```
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        2 Dec 17
                  The CA Lexicon available in the CAPLUS and CA files
           Feb 06 Engineering Information Encompass files have new names
  NEWS 4
           Feb 16 TOXLINE no longer being updated
  NEWS 5 Apr 23 Search Derwent WPINDEX by chemical structure
  NEWS 6 Apr 23
                   PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
  NEWS 7
          May 07
                  DGENE Reload
  NEWS EXPRESS May 23 CURRENT WINDOWS VERSION IS V6.0a,
                CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP),
                AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
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FILE 'HOME' ENTERED AT 00:11:11 ON 11 JUN 2001
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COST IN U.S. DOLLARS
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                                                      ENTRY
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                                                                  0.21
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for details.
=> s 87075-17-0/rn or 87134-87-0/rn or 125941-87-9/rn
             1 87075-17-0/RN
             1 87134-87-0/RN
             1 125941-87-9/RN
L1
             3 87075-17-0/RN OR 87134-87-0/RN OR 125941-87-9/RN
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=> d tot

1

ANSWER 1 OF 3 REGISTRY COPYRIGHT 2001 ACS

125941-87-9 REGISTRY

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1H-3-Benzazepin-7-ol, 8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-,
     hydrochloride, (5R) - (9CI) (CA INDEX NAME)
    1H-3-Benzazepin-7-ol, 8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-,
     hydrochloride, (R)-
OTHER NAMES:
CN Sch 23390 hydrochloride
FS
     STEREOSEARCH
MF
     C17 H18 Cl N O . Cl H
SR
LC
     STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL
         (*File contains numerically searchable property data)
CRN
     (87075-17-0)
Absolute stereochemistry. Rotation (+).
        # HC1
              53 REFERENCES IN FILE CA (1967 TO DATE)
              53 REFERENCES IN FILE CAPLUS (1967 TO DATE)
L1
     ANSWER 2 OF 3 REGISTRY COPYRIGHT 2001 ACS
     87134-87-0 REGISTRY
RN
     1H-3-Benzazepin-7-ol, 8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-,
     (5R)-, (2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     1H-3-Benzazepin-7-ol, 8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-,
     (R)-, (Z)-2-butenedioate (1:1) (salt)
OTHER NAMES:
    Sch 23390 maleate
FS
     STEREOSEARCH
DR
     121254-28-2
MF
     C17 H18 Cl N O . C4 H4 O4
     STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CSCHEM,
      DDFU, DRUGU, EMBASE, IPA, TOXLINE, TOXLIT, USPATFULL
     CM
         1
     CRN 87075-17-0
     CMF C17 H18 C1 N O
Absolute stereochemistry. Rotation (+).
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CM 2

CRN 110-16-7 CMF C4 H4 O4

Double bond geometry as shown.

609 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
609 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2001 ACS

RN 87075-17-0 REGISTRY

CN 1H-3-Benzazepin-7-ol, 8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-, (5R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-3-Benzazepin-7-ol, 8-chloro-2, 3, 4, 5-tetrahydro-3-methyl-5-phenyl-, (R) - OTHER NAMES:

CN R-(+)-Sch 23390

CN Sch 23390

FS STEREOSEARCH

MF C17 H18 Cl N O

CI COM

LC STN Files: AGRICOLA, BEILSTEIN\*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, DRUGUPDATES, MEDLINE, PHAR, PROMT, RTECS\*, TOXLINE, TOXLIT, USPATFULL

(\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

215 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

215 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s haloperidol/cn

**\_**2

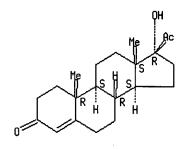
1 HALOPERIDOL/CN

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=> d
L2
    ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN
     52-86-8 REGISTRY
     1-Butanone, 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-
     fluorophenyl) - (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Butyrophenone, 4-[4-(p-chlorophenyl)-4-hydroxypiperidino]-4'-fluoro- (6CI,
     8CI)
OTHER NAMES:
    γ-[4-(p-Chlorphenyl)-4-hydroxypiperidino]-p-fluorbutyrophenone
    1-(3-p-Fluorobenzoylpropyl)-4-p-chlorophenyl-4-hydroxypiperidine
     4-(4-Hydroxy-4'-chloro-4-phenylpiperidino)-4'-fluorobutyrophenone
CN
     4-[4-(p-Chlorophenyl)-4-hydroxypiperidino]-4'-fluorobutyrophenone
CN
    Aloperidin
    Haldol
CN
CN
    Haloperidol
CN
    Haloperin
CN
    Neurodol
CN
    R 1625
CN
    Serenace
CN
     Serenase
CN
     Serenelfi
FS
     3D CONCORD
MF
     C21 H23 C1 F N 02
CI
     COM
LC
     STN Files:
                 AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*,
      HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*,
      MSDS-OHS, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT,
      USAN, USPATFULL, VETU
         (*File contains numerically searchable property data)
    Other Sources: EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
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7452 REFERENCES IN FILE CA (1967 TO DATE)
43 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7453 REFERENCES IN FILE CAPLUS (1967 TO DATE)
78 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> s "17-hydroxyprogesterone"/cn
L3
             1 "17-HYDROXYPROGESTERONE"/CN
=> d
L3
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
    68-96-2 REGISTRY
    Pregn-4-ene-3,20-dione, 17-hydroxy- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN
    \Delta 4-Pregnen-17\alpha-ol-3,20-dione
CN
    17-Hydroxypregn-4-ene-3,20-dione
CN
    17-Hydroxyprogesterone
CN
    17α-Hydroxypregn-4-ene-3,20-dione
CN
     17α-Hydroxyprogesterone
CN
     Gestageno Gador
CN
    Hydroxyprogesterone
CN
     Pregn-4-en-17\alpha-ol-3,20-dione
CN
     Prodix
CN
    Prodox
CN
     U 3096
FS
     STEREOSEARCH
DR
     67085-08-9
MF
     C21 H30 O3
CI
     COM
LC
     STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE,
       HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT,
       NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL,
       VETU
         (*File contains numerically searchable property data)
     Other Sources: EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

Absolute stereochemistry.



3425 REFERENCES IN FILE CA (1967 TO DATE)
40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3427 REFERENCES IN FILE CAPLUS (1967 TO DATE)
26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> fil medline caplus embase biosis uspatfull
COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
16.58
16.79

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=> s l1 or "sch23390" L4 10322 L1 OR "SCH23390"

=> s l2 or haloperidol or Haldol or "R 1625" or Haloperin L5 73503 L2 OR HALOPERIDOL OR HALDOL OR "R 1625" OR HALOPERIN

=> s 13 or "17-hydroxyprogesterone" or "17-Hydroxypregn-4-ene-3,20-dione"
L6 11446 L3 OR\"17-HYDROXYPROGESTERONE" OR "17-HYDROXYPREGN-4-ENE-3,20-DI
ONE"

=> s 16 and (14 or 15) L7 26 L6 AND (L4 OR L5)

=> e atherosclerosis/ct

ADDITIONAL TERMS AVAILABLE BY USING "ATHEROSCLEROSIS+XUSE/CT"

E#	FREQUENCY	ΑT	TERM
E1	0	2	ATHEROSCLEROSES, CORONARY/CT
E2	0	2	ATHEROSCLEROSES, INTRACRANIAL/CT
E3	56188	33>	ATHEROSCLEROSIS/CT
E4	0	9	ATHEROSCLEROSIS (L) FATTY STREAK/CT
E5	1		ATHEROSCLEROSIS ABSENCE/CT
E6	1		ATHEROSCLEROSIS ANTIGEN/CT
E7	1		ATHEROSCLEROSIS ASSOCIATION/CT
E8	1		ATHEROSCLEROSIS BURDEN CORRELATED/CT
E9	1		ATHEROSCLEROSIS CANDIDATE GENE/CT
E10	0	2	ATHEROSCLEROSIS CEREBRI/CT
E11	1		ATHEROSCLEROSIS CHANGE EFFECT/CT
E12	1	`	ATHEROSCLEROSIS CONTRIBUTION/CT

=> e e3+all

'ALL' IS NOT VALID HERE

ADDITIONAL TERMS AVAILABLE BY USING "ATHEROSCLEROSIS+XUSE/CT"

E#	FREQUENCY	AT	TERM
E13	0	2	ATHEROSCLEROSES, CORONARY/CT
E14	0	2	ATHEROSCLEROSES, INTRACRANIAL/CT
E15	56188	33:	> ATHEROSCLEROSIS/CT
E16	0	9	ATHEROSCLEROSIS (L) FATTY STREAK/CT
E17	1		ATHEROSCLEROSIS ABSENCE/CT
E18	1	•	ATHEROSCLEROSIS ANTIGEN/CT
E19	1		ATHEROSCLEROSIS ASSOCIATION/CT
E20	1		ATHEROSCLEROSIS BURDEN CORRELATED/CT
E21	1		ATHEROSCLEROSIS CANDIDATE GENE/CT
E22	0	2	ATHEROSCLEROSIS CEREBRI/CT

E23 1 ATHEROSCLEROSIS CHANGE EFFECT/CT
E24 1 ATHEROSCLEROSIS CONTRIBUTION/CT
Relationship codes are not available in multifile sessions.

=> s atheroscler? or arteroscler? or hard? arter?

L8 179300 ATHEROSCLER? OR ARTEROSCLER? OR HARD? ARTER?

=> s 18 and 17

L9 3 L8 AND L7

=> d tot ibib abs kwic

L9 ANSWER 1 OF 3 MEDLINE

Full-text

ACCESSION NUMBER: 2001098345 MEDLINE

DOCUMENT NUMBER: 20582286 PubMed ID: 11146301

TITLE: Serum lipids and arterial plaque load are altered

independently with high-dose progesterone in

hypercholesterolemic male rabbits.

AUTHOR: Houser S L; Aretz H T; Quist W C; Chang Y; Schreiber A D

CORPORATE SOURCE: Department of Pathology, Massachusetts General Hospital,

Harvard Medical School, Boston, MA, USA..

houser.stuart@mgh.harvard.edu

SOURCE: CARDIOVASCULAR PATHOLOGY, (2000 Nov-Dec) 9 (6) 317-22.

Journal code: DGK. ISSN: 1054-8807.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322 Entered PubMed: 20010116 Entered Medline: 20010201

AB Antiatherogenic effects of sex steroids in premenopausal women are not well defined. Therefore, we employed an established rabbit model for atherosclerosis to study the effects of exogenous estrogen and a progesterone analogue (P) on serum lipids and aortic plaque load. Serum cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque loads were compared in 5 groups of male New Zealand White rabbits fed a 12-week, C-rich diet: 1 control group (CG) and 4 groups treated with estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the LDP and HDP groups. Serial histologic sections (15 each of 27 ascending aortas) were studied by light microscopy and computerized morphometric analysis. Plaque load is defined as the ratio of intimal area to medial area (I/M). Exogenous E (p<0.001), H (P = 0.02), LDP and HDP (P<0.001, each) were found to be significantly associated with less aortic plaque load than controls. In a multivariate analysis, after controlling for the differences in serum C and T levels, HDP (p = 0.014) was found to be associated with less aortic plaque load than controls, and this association approached statistical significance in the E (p = 0.052) and H (p = 0.069) groups. These data suggest that the mechanism(s) involved with the antiatherogenic effect of HDP in this animal model is, or are, independent of an alteration in serum lipids.

Antiatherogenic effects of sex steroids in premenopausal women are not well defined. Therefore, we employed an established rabbit model for atherosclerosis to study the effects of exogenous estrogen and a progesterone analogue (P) on serum lipids and aortic plaque load. Serum cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque loads were compared in 5 groups of male New Zealand White rabbits fed a 12-week, C-rich diet: 1 control group (CG) and 4 groups treated with

```
estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP),
     or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the
     LDP and HDP groups. Serial histologic sections (15 each of 27 ascending
     aortas). .
    Check Tags: Animal; Male
     *17-Hydroxyprogesterone: AD, administration dosage
     Aorta: DE, drug effects
   *Aorta: ME, metabolism
     Aorta: PA, pathology
     *Cholesterol: BL, blood
     Cholesterol, Dietary: AD, . . ET, etiology
     *Coronary Arteriosclerosis: ME, metabolism
     Coronary Arteriosclerosis: PA, pathology
     *Diet, Atherogenic
     Dose-Response Relationship, Drug
     Estriol: AD, administration dosage
     Haloperidol: AD, administration dosage
     *Hypercholesterolemia: BL, blood
     Hypercholesterolemia: ET, etiology
     Hypercholesterolemia: PA, pathology
     Image Processing, Computer-Assisted
     Rabbits
     *Triglycerides: BL,.
RN
     50-27-1 (Estricl); 52-86-8 (Haloperidol); 57-88-5 (Cholesterol);
     68-96-2 (17-Hydroxyprogesterone)
    ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
Full-text
ACCESSION NUMBER:
                         2001:8027 CAPLUS
DOCUMENT NUMBER:
                         134:173174
TITLE:
                         Serum Lipids and Arterial Plaque Load are Altered
                         Independently with High-Dose Progesterone in
                         Hypercholesterolemic Male Rabbits
AUTHOR (S):
                         Houser, S. L.; Aretz, H. T.; Quist, W. C.; Chang, Y.;
                         Schreiber, A. D.
CORPORATE SOURCE:
                         Department of Pathology, Massachusetts General
                         Hospital, Harvard Medical School, Boston, MA, USA
SOURCE:
                         Cardiovasc. Pathol. (2000), 9(6), 317-322
                         CODEN: CATHE8; ISSN: 1054-8807
PUBLISHER:
                         Elsevier Science Inc.
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
    Antiatherogenic effects of sex steroids in premenopausal women are not
    well defined. Therefore, we employed an established rabbit model for
     atherosclerosis, to study the effects of exogenous estrogen and a
    progesterone analog (P) on serum lipids and aortic plaque load. Serum
    cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque
    loads were compared in 5 groups of male New Zealand White rabbits fed a
    12-wk, C-rich diet: 1 control group (CG) and 4 groups treated with estriol
     (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or
    high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the
    LDP and HDP groups. Serial histol. sections (15 each of 27 ascending
    aortas) were studied by light microscopy and computerized morphometric
    anal. Plaque load is defined as the ratio of intimal area to medial area
     (I/M). Exogenous E, H, LDP and HDP were found to be significantly assocd.
    with less aortic plaque load than controls. In a multivariate anal.,
    after controlling for the differences in serum C and T levels, HDP was
    found to be assocd. with less aortic plaque load than controls, and this
     assocn. approached statistical significance in the E (p = 0.052) and H (p = 0.052)
     = 0.069) groups. These data suggest that the mechanism(s) involved with
     the antiatherogenic effect of HDP in this animal model is, or are,
     independent of an alteration in serum lipids.
```

REFERENCE COUNT: REFERENCE(S): 49

- (1) Adams, M; Arteriosclerosis 1990, V10, P1051 CAPLUS
- (2) Alexandersen, P; Arterioscler Thromb Vasc Biol 1998, V18, P902 CAPLUS
- (7) Daley, S; Arterioscler Thromb 1994, V14, P95 CAPLUS
- (8) Dubey, R; Arterioscler Thromb Vasc Biol 2000, V20, P964 CAPLUS
- (9) Fischer, G; Atherosclerosis 1985, V54, P177 CAPLUS ALL CITATIONS AVAILABLE IN THE RE FORMAT
- Antiatherogenic effects of sex steroids in premenopausal women are not well defined. Therefore, we employed an established rabbit model for atherosclerosis to study the effects of exogenous estrogen and a progesterone analog (P) on serum lipids and aortic plaque load. Serum cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque loads were compared in 5 groups of male New Zealand White rabbits fed a 12-wk, C-rich diet: 1 control group (CG) and 4 groups treated with estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the LDP and HDP groups. Serial histol. sections (15 each of 27 ascending aortas) were studied by light microscopy and computerized morphometric anal. Plaque load is defined as the ratio of intimal area to medial area (I/M). Exogenous E, H, LDP and HDP were found to be significantly assocd. with less aortic plaque load than controls. In a multivariate anal., after controlling for the differences in serum C and T levels, HDP was found to be assocd. with less aortic plaque load than controls, and this assocn. approached statistical significance in the E (p = 0.052) and H (p = 0.052) = 0.069) groups. These data suggest that the mechanism(s) involved with the antiatherogenic effect of HDP in this animal model is, or are, independent of an alteration in serum lipids.

### IT Atherosclerosis

Hypercholesterolemia

(serum lipids and arterial plaque load are altered independently with high-dose hydroxyprogesterone in hypercholesterolemic male rabbits)

# IT 52-86-8, Haloperidol

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(hydroxyprogesterone and haloperidol effect on serum lipids and arterial plaque load in hypercholesterolemic male rabbits)

# IT 68-96-2, 17-Hydroxyprogesterone

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (serum lipids and arterial plaque load are altered independently with high-dose hydroxyprogesterone in hypercholesterolemic male rabbits)

L9 ANSWER 3 OF 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

Full-text

ACCESSION NUMBER: 2001008975 EMBASE

TITLE: Serum lipids and arterial plaque load are altered

independently with high-dose progesterone in

hypercholesterolemic male rabbits.

AUTHOR: Houser S.L.; Aretz H.T.; Quist W.C.; Chang Y.C.; Schreiber

A.D.

CORPORATE SOURCE: Dr. S.L. Houser, Department of Pathology, Massachusetts

General Hospital, Fruit Street, Boston, MA 02114, United

States. houser.stuart@mgh.harvard.edu

SOURCE: Cardiovascular Pathology, (2000) 9/6 (317-322).

Refs: 49

ISSN: 1054-8807 CODEN: CATHE8

PUBLISHER IDENT.: S 1054-8807(00)00051-X

COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 002 Physiology

029 Clinical Biochemistry

Q30 Pharmacology

037 Drug Literature Index

005 General Pathology and Pathological Anatomy

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Antiatherogenic effects of sex steroids in premenopausal women are not well defined. Therefore, we employed an established rabbit model for atherosclerosis to study the effects of exogenous estrogen and a progesterone analogue (P) on serum lipids and aortic plaque load. Serum cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque loads were compared in 5 groups of male New Zealand White rabbits fed a 12-week, C-rich diet: 1 control group (CG) and 4 groups treated with estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the LDP and HDP groups. Serial histologic sections (15 each of 27 ascending aortas) were studied by light microscopy and computerized morphometric analysis. Plaque load is defined as the ratio of intimal area to medial area (I/M). Exogenous E (p < 0.001), H (P = 0.02), LDP and HDP (P < 0.001, each) were found to be significantly associated with less aortic plaque load than controls. In a multivariate analysis, after controlling for the differences in serum C and T levels, HDP (p = 0.014) was found to be associated with less aortic plaque load than controls, and this association approached statistical significance in the E (p = 0.052) and H (p = 0.069) groups. These data suggest that the mechanism(s) involved with the antiatherogenic effect of HDP in this animal model is, or are, independent of an alteration in serum lipids. Copyright © 2000 Elsevier Science Inc.

AB Antiatherogenic effects of sex steroids in premenopausal women are not well defined. Therefore, we employed an established rabbit model for atherosclerosis to study the effects of exogenous estrogen and a progesterone analogue (P) on serum lipids and aortic plaque load. Serum cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque loads were compared in 5 groups of male New Zealand White rabbits fed a 12-week, C-rich diet: 1 control group (CG) and 4 groups treated with estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the LDP and HDP groups. Serial histologic sections (15 each of 27 ascending aortas).

CT Medical Descriptors:

\*atherosclerotic plaque

\*hypercholesterolemia: DT, drug therapy

rabbit

lipid blood level

triacylglycerol blood level

cholesterol blood level

male

animal model

tissue section

histology

multivariate analysis

morphometrics

microscopy

nonhuman

controlled study

animal tissue

article

priority journal

\*estriol: DT, drug therapy

\*estriol:. . subcutaneous drug administration

\*hydroxyprogesterone: PK, pharmacokinetics

\*hydroxyprogesterone: DT, drug therapy

\*hydroxyprogesterone: DO, drug dose \*hydroxyprogesterone: CR, drug concentration \*hydroxyprogesterone: CM, drug comparison \*hydroxyprogesterone: SC, subcutaneous drug administration haloperidol: DT, drug therapy haloperidol: CM, drug comparison haloperidol: SC, subcutaneous drug administration (estriol) 50-27-1; (hydroxyprogesterone) 68-96-2; (haloperidol) 52-86-8 => s 17 and cardiovascular 6 L7 AND CARDIOVASCULAR => dup rem 110 PROCESSING COMPLETED FOR L10 6 DUP REM L10 (0 DUPLICATES REMOVED) => d ibib abs kwic tot L11 ANSWER 1 OF 6 USPATFULL <u>Full-text</u> ACCESSION NUMBER: 2001:55484 USPATFULL TITLE: Self adjustable exit port INVENTOR (S): Gumucio, Juan C., Santa Clara, CA, United States Dionne, Keith E., Cambridge, MA, United States Brown, James E., Los Gatos, CA, United States PATENT ASSIGNEE(S): ALZA Corporation, Mountain View, CA, United States (U.S. corporation) NUMBER DATE \_\_\_\_\_\_ PATENT INFORMATION: US 6217906 20010417 US 1999-397507 19990917 (9) APPLICATION INFO.: Division of Ser. No. US 1998-45944, filed on 23 Mar RELATED APPLN. INFO.: 1998, now patented, Pat. No. US 5997527 NUMBER DATE -----PRIORITY INFORMATION: 19970324 (60) US 1997-35607 DOCUMENT TYPE: Utility PRIMARY EXAMINER: Page, Thurman K. ASSISTANT EXAMINER: Tran, S. LEGAL REPRESENTATIVE: Clarke, Pauline A.; Mukai, Robert G.; Stone, Steven F. NUMBER OF CLAIMS: EXEMPLARY CLAIM: NUMBER OF DRAWINGS: 9 Drawing Figure(s); 7 Drawing Page(s) LINE COUNT: 1128 A delivery device having a first chamber containing an osmotic agent, a membrane forming a wall of the first chamber through which fluid is imbibed by osmosis, a second chamber containing a beneficial agent to be delivered, and a moveable piston separating the two chambers. In fluid communication with the second chamber is an orifice which comprises a slit valve. In the presence of pressure, the beneficial agent pushes through the slit, opening up a channel for delivery of the beneficial agent and creating flow. Because the slit remains closed in the absence of flow (or when the pressure is below the pressure required to open the slit), back diffusion of external fluids is eliminated when the slit is closed, which prevents contamination of the beneficial agent in the second chamber by external fluids. In addition, forward diffusion of the beneficial agent out of the capsule is prevented when the slit is

closed. The slit valve opens only to the minimum dimension required to

allow the flow generated by the osmotic pumping rate. The slit valve also allows a flow path to open around any obstruction in the slit valve to prevent clogging.

DETD . . . by the present invention include drugs which act on the peripheral nerves, adrenergic receptors, cholinergic receptors, the skeletal muscles, the cardiovascular system, smooth muscles, the blood circulatory system, synoptic sites, neuroeffector junctional sites,

endocrine and hormone systems, the immunological system, the. . . DETD

. . acetate, cortisone acetate, dexamethasone and its derivatives such as betamethasone, triamcinolone, methyltestosterone, 17-S-estradiol, ethinyl estradiol, ethinyl estradiol 3-methyl ether, prednisolone, 17-hydroxyprogesterone acetate, 19-nor-progesterone, norgestrel, norethindrone, norethisterone, norethiederone, progesterone, norgesterone, norethynodrel, aspirin, indomethacin, naproxen, fenoprofen, sulindac, indoprofen, nitroglycerin, isosorbide dinitrate, propranolol, timolol, atenolol, alprenolol, cimetidine, clonidine, imipramine, levodopa, chlorpromazine, methyldopa, dihydroxyphenylalanine, theophylline, calcium gluconate, ketoprofen, ibuprofen, cephalexin, erythromycin, haloperidol, zomepirac, ferrous lactate, vincamine, diazepam, phenoxybenzamine, diltiazem, milrinone, capropril, mandol, quanbenz, hydrochlorothiazide, ranitidine, flurbiprofen, fenufen, fluprofen, tolmetin, alclofenac, mefenamic, flufenamic, . . .

## L11 ANSWER 2 OF 6 USPATFULL

Full-text

ACCESSION NUMBER: 2001:17714 USPATFULL

TITLE: Dosage form comprising a capsule

INVENTOR(S): Wong, Patrick S. L., Burlingame, CA, United States

Theeuwes, Felix, Los Altos Hills, CA, United States Ferrari, Vincent J., Foster City, CA, United States

Dong, Liang C., Sunnyvale, CA, United States

PATENT ASSIGNEE(S): Alza Corporation, Mountain View, CA, United States

(U.S. corporation)

NUMBER DATE

PATENT INFORMATION: US 6183466 20010206

APPLICATION INFO.: US 1999-344811 19990625 (9)

NUMBER DATE PRIORITY INFORMATION: US 1998-97390 19980821 (60)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Page, Thurman K. ASSISTANT EXAMINER: Pulliam, Amy E.

LEGAL REPRESENTATIVE: Dhuey, John A.; Stone, Steven F.

NUMBER OF CLAIMS: 7 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 641

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A dosage form is disclosed comprising a wall that defines an injection-molded compartment housing a capsule comprising a drug formulation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

. . . organic compounds without limitation, including drugs that act on the peripheral nerves, adrenergic receptors, cholinergic receptors, nervous system, skeletal muscles, cardiovascular system, smooth muscles, blood circulatory system, synoptic sites, neuroeffector

junctional sites, endocrine system, hormone systems, immunological system, organ systems, reproductive. . . analgesics, anti-inflammatories, local anesthetics, muscle contractants, antimicrobials, anti-malarials, hormonal agents, contraceptives, sympathomimetics, diuretics, anti-parasitics, neoplastics, hypoglycemics, opthalmics, electrolytes, diagnostic agents, cardiovascular drugs, and the like.

DETD

. . . progestins, estrogenic progestational, corticosteroids, hydrocortisone, hydrocorticosterone acetate, cortisone acetate, triamcinolone, methyltesterone, 17  $\beta$ -estradiol, ethinyl estradiol, ethinyl estradiol 3-methyl ether, prednisolone, 17hydroxyprogesterone acetate, 19-norprogesterone, norgestrel, norethindone, norethiderone, progesterone, norgesterone, norethynodrel, enitabas, indomethacin, naproxen, fenoprofen, sulidac, diclofenac, indoprofen, nitroglycerin, propranolol, metoprolol, valproate, oxprenolol,. . . imipramine, levodopa, chloropmpmazine, reserpine, methyl-dopa, dihydroxyphenylalanine, pivaloyloxyethyl ester of  $\alpha$ -methyldopa hydrochloride, theophylline, calcium gluconate ferrous lactate, ketoprofen, ibuprofen, cephalexin, erythromycin, haloperidol, zomepirac, vincamine, diazepam, phenoxybenzamine,  $\beta$ -blocking agents, calcium-channel blocking drugs such as nifedipine, diltiazen, verapamil, and the like. The beneficial drugs. .

# L11 ANSWER 3 OF 6 USPATFULL

Full-text

INVENTOR(S):

ACCESSION NUMBER: 2000:98025 USPATFULL

TITLE:

Dosage form, process of making and using same Ayer, Atul D., Palo Alto, CA, United States Lam, Andrew, San Francisco, CA, United States

Magruder, Judy A., Mountain View, CA, United States Hamel, Lawrence G., Mountain View, CA, United States Wong, Patrick S. L., Palo Alto, CA, United States

PATENT ASSIGNEE(S):

ALZA Corporation, Mountain View, CA, United States

(U.S. corporation)

NUMBER DATE

PATENT INFORMATION:

US 6096339 20000801 US 1997-826642 19970404 (8)

APPLICATION INFO.: DOCUMENT TYPE:

Utility

PRIMARY EXAMINER: ASSISTANT EXAMINER:

Page, Thurman K. Seidleck, Brian K.

LEGAL REPRESENTATIVE:

Sabatine, Paul L.; Thomas, Susan K.

NUMBER OF CLAIMS:

31

EXEMPLARY CLAIM:

3 Drawing Figure(s); 3 Drawing Page(s)

NUMBER OF DRAWINGS:

LINE COUNT:

1277

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention disclosed pertains to a dosage form comprising an agent formulation comprising drug and pharmaceutical carrier of cooperating particle size and means for dispensing the agent formulation from the dosage form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

. . organic compounds without limitation, including drugs that act on the peripheral nerves, adrenergic receptors, cholinergic receptors, nervous system, skeletal muscles, cardiovascular system, smooth muscles, blood circulatory system, synoptic sites, neuroeffector junctional sites, endocrine system, hormone systems, immunological system, organ systems, reproductive. . . anti-inflammatories, polypeptides, local anesthetics, muscle contractants, antimicrobials,

antimalarials, hormonal agents, contraceptives, sympathomimetics, diuretics, antiparasitics, neoplastics, hypoglycemics, ophthalmics, electrolytes, diagnostic agents, cardiovascular drugs, calcium channel blockers, angiotensin converting enzyme inhibitors, and the like. DETD . . . sulfisoxazole, erythromycin, progestins, estrogenic progestational, corticosteroids, hydrocortisone acetate, cortisone acetate, triamcinolone, methyltestosterone, 17\beta-estradiol, ethinyl estradiol, ethinyl estradiol 3-methyl ether, prednisolone, 17-hydroxyprogesterone acetate, 19-nor-progesterone, norgestrel, norethindrone, norethisterone, progesterone, norgesterone, norethyndral, aspirin, indomethacin, aproxen, fenoprofen, sulindac, diclofenac, indoprofen, nitroglycerin, propranolol, metoprolol, valproate, oxprenolol, . . . clonidine, imipramine, levodopa, chlorpromazine, methyldopa, dihydroxyphenylalanine, pivaloyloxyethyl ester of ε-methyldopa hydrochloride, theophylline, calcium gluconate ferrous lactate, ketoprofen, ibuprofen, cephalexin, erythromycin, haloperidol, zomepirac, vincamine, diazepam, phenoxybenzamine,  $\beta$ -blocking agents; calcium-channel blocking drugs, such as nifedipine, diltiazem, isradipine, nilvadipine, verapamil, flunarizine, nimodipine, felodipine, amlodipine,.

# L11 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS

Full-text

ACCESSION NUMBER: 1995:833169 CAPLUS

DOCUMENT NUMBER: 123:237824

TITLE:

Transdermal drug delivery system containing polyvinylpyrrolidone as solubility enhancer

Miranda, Jesus; Sablotsky, Steven

PATENT ASSIGNEE(S):

Noven Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 74 pp. CODEN: PIXXD2

DOCUMENT TYPE:

INVENTOR(S):

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

					KIND DATE								DATE						
	9518603				 1	19950713			WO 1995-US22						 0109				
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														SI,					
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						19950713 19950801													
									Z	ZA 1995-108				1995	19950109				
EP	7370	66		A1		19961016			EP 1995-906742					1995	0109				
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CN	1143															,	,		
	7491																		
									BR 1995-6470 JP 1995-518540										
									FI 1996-2770										
	9923																		
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	6221	383		В	l .	2001	0424	1	US 1	S 19 994-	99-3: 1785:	1812 58	1 A	1999	0525 0107				

WO 1995-US22 . W 19950109 US 1997-907906 A3 19970811 A blend of at least three polymers, including a sol. PVP, in combination with a drug provides a pressure-sensitive adhesive compn. for a transdermal drug delivery system in which the drug is delivered through dermis when it is in contact with human skin. Sol. PVP increases the soly. of drug without neg. affecting the adhesivity of the compn. or the rate of drug delivery from the pressure-sensitive adhesive compn. A transdermal drug delivery system contained polysiloxane adhesive (BIO-PSA Q7-4503) 40.0, polyacrylate adhesive (GMS 737) 40.0, oleic acid 8.0, dipropylene glycol 6.0, PVP 5.0, and estradiol 1%. TΤ Adrenergic agonists Analgesics Anesthetics Cardiovascular agents Cholinergic agonists Neoplasm inhibitors Nervous system agents Tranquilizers and Neuroleptics

Vasodilators

(transdermal drug delivery system contg. polyvinylpyrrolidone as soly. enhancer)

50-27-1, Estriol 50-36-2, Cocaine 50-52-2, Thioridazine Chlorpromazine, biological studies 50-54-4, Quinidine sulfate Procainamide 51-83-2, Carbachol 51-84-3, Acetylcholine, biological studies 51-98-9, Norethindrone acetate 52-53-9, Verapamil 52-76-6 52-86-8, Haloperidol 54-11-5, Nicotine 55-63-0, Nitroglycerin 55-92-5, Methacholine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol 57-83-0, Progesterone, biological studies 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-74-2, Papaverine 58-94-6, Chlorothiazide 58-95-7, Vitamin e acetate 59-46-1, Procaine 62-49-7, Choline 68-22-4, Norethindrone 68-23-5, Norethynodrel 68-96-2,  $17\alpha$ -Hydroxyprogesterone 69-23-8, Fluphenazine 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol Benzhydroflumethiazide 76-57-3, Codeine 79-64-1, Dimethisterone 84-06-0, Thiopropazate 85-79-0, Dibucaine 87-33-2, Isosorbide dinitrate 92-13-7, Pilocarpine 94-09-7, Benzocaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 106-60-5,  $\delta$ -Aminolevulinic acid 113-59-7, Chlorprothixene 117-89-5, Trifluoperazine 137-58-6, Lidocaine 146-54-3, Triflupromazine 152-62-5, Dydrogesterone 297-76-7, Ethynodiol diacetate 300-54-9, Muscarine 434-03-7, Ethisterone 437-38-7, Fentanyl 439-14-5, Diazepam 472-54-8, 19-Norprogesterone 474-86-2, Equilin 525-66-6, Propranolol 586-06-1, MetaProterenol 586-60-7, Dyclonine 595-33-5, Megestrol acetate 604-75-1, Oxazepam 630-56-8, Hydroxypro-gesterone caproate Bethanechol 721-50-6, Prilocaine 846-49-1, Lorazepam 1622-61-3, Clonazepam 1961-77-9, Chlormadinone 1977-10-2, Loxapine 2180-92-9, Bupivacaine 2751-68-0, Acetophenazine 2955-38-6, Prazepam Thiothixene 3819-00-9, Piperacetazine 4205-90-7, Clonidine 5588-33-0, Mesoridazine 5633-18-1, Melengestrol 6533-00-2, Norgestrel 7280-37-7, Estropipate 7416-34-4, Molindone 9003-39-8, Polyvinylpyrrolidone 10116-22-0, Demegestone 10457-90-6, Bromperidol 13392-18-2, Fenoterol 13642-52-9, Soterenol 13757-97-6, Quinterenol 14611-51-9, Selegiline 16051-77-7, Isosorbide mononitrate 17617-23-1, Flurazepam 18559-94-9, Albuterol 18910-65-1, Salmefamol 19216-56-9, Prazosin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 23031-25-6, Terbutaline 23092-17-3, Halazepam 23887-31-2, Clorazepate 26839-75-8, Timolol 28911-01-5, Triazolam 28981-97-7, Alprazolam 32953-89-2, Rimiterol 34184-77-5, Promegestone 34866-47-2, Carbuterol 36637-18-0, Etidocaine 42399-41-7, Diltiazem 52485-79-7, Buprenorphine 55985-32-5, Nicardipine 62571-86-2, Captopril RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(transdermal drug delivery system contg. polyvinylpyrrolidone as soly. enhancer)

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L11 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2001 ACS
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Full-text

ACCESSION NUMBER:

1993:154566 CAPLUS

DOCUMENT NUMBER:

118:154566

TITLE:

Solubility parameter-based transdermal drug delivery

system and method for altering drug saturation

concentration

INVENTOR(S): PATENT ASSIGNEE(S): Miranda, Jesus; Sablotsky, Steven Noven Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.  WO 9300058			KI						PPLI	CATI	DATE					
WO				A1 19930107						0 19	92-U	- <i>-</i> -	19920622				
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		KR,	LK,	LU,	MG,	MW,	NL,	NO,	PL,	RO,	RU,	SD,	SE				
	RW:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LU,	MC,	NL,	SE		
CA	21109	14		A	A	1993	0107		С	A 19	92-2	1109	14	1992	0622		
AU	92226	89		A	1	1993	0125		Α	U 19	92-2	2689		1992	0622		
AU	67003	3		B	2	1996	0704										
EP	59143	32		A	1	1994	0413		E	P 19	92-9	1485	5	1992	0622		
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	92062																
RU	21243	40		C	1	1999	0110		R	U 19	93-5	8609		1992	0622		
IL	10227	77		A.	1	2000	0716		I	L 19	92-1	0227	7	1992	0622		
ZA	92099	92		A		1994	0623		Z	A 19	92-99	992		1992	1223		
	10887																
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US	62353	06		B	l.	2001	0522		· U	S 19	99-2	74886	5	1999	0323		
PRIORITY	APPL	ın. I	NFO.	:				τ	JS 1	991-	72234	12	Α	1991	0627		
								V	VO 1	992-	US52	97	Α	1992	0622		
								τ	JS 1	995-	4337	54	A1	1995	0504		

A transdermal drug delivery system comprises  $\geq$  2 polymers having differing soly. parameters. The preferred system is a pressure-sensitive adhesive matrix for controlled drug delivery. The characteristic net soly. parameter can be preselected to adjust the satn. concn. of the drug, and thereby control its release. A compn. comprised nitroglycerin 22.0, Silicone Adhesive X7-4919 42.8, Duro-Tak 80-1194 (acrylic adhesive) 28.6, dimethylsiloxane fluid 2.5, lecithin 1.3, propylene glycol 0.8, dipropylene glycol 1.0, and bentonite 1.0 %. The nitroglycerin flux from this compn. through cadaver skin was twice that from com. Transderm-Nitro and 1.5 times that from Nitro-Dur.

ΙT Analgesics

Anesthetics

Cardiovascular agents

Cholinergic agonists

Nervous system agents

Tranquilizers and Neuroleptics

Estrogens

Progestogens

RL: BIOL (Biological study)

(transdermal pressure-sensitive adhesive delivery system for, controlled-release)

ΙT 50-27-1, Estriol 50-28-2,  $17\beta$ -Estradiol, biological studies

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50-36-2, Cocaine 50-52-2, Thioridazine 50-53-3, Chlorpromazine,
    biological studies 50-54-4, Quinidine sulfate 51-06-9, Procainamide
    51-83-2, Carbachol 51-84-3, Acetylcholine, biological studies 51-98-9,
    Norethindrone acetate 52-53-9, Verapamil 52-76-6 52-86-8,
    Haloperidol 53-16-7, Estrone, biological studies 54-11-5,
    Nicotine 55-63-0, Nitroglycerin 55-92-5, Methacholine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol 57-83-0, Progesterone,
    biological studies 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine
    58-94-6, Chlorothiazide 59-46-1, Procaine 62-49-7, Choline 63-75-2,
    Arecoline 68-22-4, Norethindrone 68-23-5, Norethynodrel
    68-96-2, 17-Hydroxyprogesterone 69-23-8,
    Fluphenazine 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol
    73-48-3, Bendroflumethiazide 76-57-3, Codeine 79-64-1, Dimethisterone
    84-06-0, Thiopropazate 85-79-0, Dibucaine 87-33-2, Isosorbide
    dinitrate 92-13-7, Pilocarpine 94-09-7, Benzocaine 94-24-6,
    Tetracaine 96-88-8, Mepivacaine 113-59-7 117-89-5, Trifluoperazine
    137-58-6, Lidocaine 146-54-3, Triflupromazine 152-62-5, Dydrogesterone
    297-76-7, Ethynodiol diacetate 300-54-9, Muscarine 434-03-7,
    Ethisterone 437-38-7, Fentanyl 439-14-5, Diazepam 472-54-8,
    19-Norprogesterone 474-86-2, Equilin 525-66-6, Propranolol 586-06-1,
    Metaproterenol 586-60-7, Dyclonine 595-33-5, Megestrol acetate
    604-75-1, Oxazepam 630-56-8 721-50-6, Prilocaine 846-49-1, Lorazepam
    1622-61-3, Clonazepam 1961-77-9, Chlormadinone 1977-10-2, Loxapine
    2180-92-9, Bupivacaine 2751-68-0, Acetophenazine 2955-38-6, Prazepam
    3819-00-9, Piperacetazine 4205-90-7, Clonidine 5588-33-0, Mesoridazine
    5591-45-7, Thiothixene 5633-18-1, Melengestrol 6533-00-2, Norgestrel
    7280-37-7, Estropipate 7416-34-4, Molindone 10116-22-0, Demegestone
    10457-90-6, Bromperidol 13392-18-2, Fenoterol 13642-52-9, Soterenol
    13757-97-6, Quinterenol 16051-77-7, Isosorbide mononitrate 17617-23-1,
    Flurazepam 18559-94-9, Albuterol 18910-65-1, Salmefamol 19216-56-9,
    Prazosin 21829-25-4, Nifedipine 23031-25-6, Terbutaline 23092-17-3,
    Halazepam 23887-31-2 26839-75-8, Timolol 28911-01-5, Triazolam
    28981-97-7, Alprazolam 30418-38-3, Tretoquinol 32953-89-2, Rimiterol
    34184-77-5, Promegestone 34866-47-2, Carbuterol 36637-18-0, Etidocaine
    42399-41-7, Diltiazem 52485-79-7, Buprenorphine 55985-32-5,
    Nicardipine 62571-86-2, Captopril 91609-06-2, Betanechol
    RL: BIOL (Biological study)
       (transdermal pressure-sensitive adhesive delivery system for,
       controlled-release)
L11 ANSWER 6 OF 6 USPATFULL
```

Full-text

ACCESSION NUMBER: 86:69547 USPATFULL

TITLE:

Osmotic capsule

INVENTOR (S):

Deters, Joseph C., Mountain View, CA, United States Theeuwes, Felix, Los Altos, CA, United States

Mullins, Kevin J., Berkeley, CA, United States Eckenhoff, James B., Los Altos, CA, United States

PATENT ASSIGNEE(S): ALZA Corporation, Palo Alto, CA, United States (U.S.

corporation)

NUMBER DATE -----US 4627850 19861209

US 1983-548219 19831102 (6)

PATENT INFORMATION: APPLICATION INFO.:

DOCUMENT TYPE: Utility Schofer, Joseph L. PRIMARY EXAMINER:

ASSISTANT EXAMINER: Teskin, F. M. LEGAL REPRESENTATIVE: Sabatine, Paul L.; Mandell, Edward L.; Stone, Steven F.

26

NUMBER OF CLAIMS:

NUMBER OF DRAWINGS:

EXEMPLARY CLAIM:

8 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 1200

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An osmotic capsule is disclosed for delivering a beneficial agent formulation to an environment of use. The osmotic capsule comprises an outer semipermeable wall surrounding and laminating an inner capsule wall formed of a different polymeric composition than the outer wall. The walls define an interior space containing the beneficial agent formulation. A passageway through the walls connects the exterior of the osmotic capsule with the interior of the osmotic capsule.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . organic compounds without limitation, including drugs that act on the peripheral nerves, adrenergic receptors, cholinergic receptors, nervous system, skeletal muscles, cardiovascular system, smooth muscles, blood circulatory system, synoptic sites, neuroeffector junctional sites, endocrine system, hormone systems, immunological system, organ systems, reproductive. . . analgesics, anti-inflammatories, local anesthetics, muscle contractants, anti-microbials, anti-malarials, hormonal agents, contraceptives, sympathomimetics, diuretics, anti-parasitics, neoplastics, hypoglycemics, ophthalmics, electrolytes, diagnostic agents, cardiovascular drugs, and the like.

DETD . . . erythromycin, progestins, estrogenic progestational, corticosteriods, hydrocortisone, hydrocorticosterone acetate, cortisone acetate, triamcinolone, methyltesterone,  $17\beta$ -estradiol, ethinyl estradiol, ethinyl estradiol 3-methyl ether, prednisolone, 17-hydroxyprogesterone acetate, 19-nor-progesterone, norgestrel, norethindone, norethiderone, progesterone, norgesterone, norethynodrel, aspirin, indomethacin, naproxen, fenoprofen, sulidac, diclofenac, indoprofen, nitroglycerin, propranolol, metoprolol, valproate, oxprenolol,. . . imipramine, levodopa, chloropropmazine, reserpine, methyl-dopa, dihydroxyphenylalanine, pivaloyloxyethyl ester of  $\alpha\text{-methyldopa}$  hydrochloride, theophylline, calcium gluconate ferrous lactate, ketoprofen, ibuprofen, cephalexin, erythromycin, haloperidol, zomepirac, vincamine, diazepam, phenoxybenzamine,  $\beta$ -blocking agents, calcium-channel blocking drugs such as nifedipine, diltiazen, verapamil, and the like. The beneficial drugs. .

=> dup rem 17
PROCESSING COMPLETED FOR L7
L12 22 DUP REM L7 (4 DUPLICATES REMOVED)

=> s 112 NOT 111 L13 16 L12 NOT L11

=> d ibib abs kwic tot

L13 ANSWER 1 OF 16 MEDLINE

<u>Full-text</u>

ACCESSION NUMBER: 2001098345 MEDLINE

DOCUMENT NUMBER: 20582286 PubMed ID: 11146301

TITLE: Serum lipids and arterial plaque load are altered independently with high-dose progesterone in

hypercholesterolemic male rabbits.

AUTHOR: Houser S L; Aretz H T; Quist W C; Chang Y; Schreiber A D CORPORATE SOURCE: Department of Pathology, Massachusetts General Hospital,

Harvard Medical School, Boston, MA, USA..

houser.stuart@mgh.harvard.edu

SOURCE: CARDIOVASCULAR PATHOLOGY, (2000 Nov-Dec) 9 (6) 317-22.

Journal code: DGK. ISSN: 1054-8807.

PUB. COUNTRY:

United States

Journal; Article; (JOURNAL ARTICLE) LANGUAGE: English FILE SEGMENT: Priority Journals ENTRY MONTH: 200102 ENTRY DATE: Entered STN: 20010322 Last Updated on STN: 20010322 Entered PubMed: 20010116 Entered Medline: 20010201 Antiatherogenic effects of sex steroids in premenopausal women are not well defined. Therefore, we employed an established rabbit model for atherosclerosis to study the effects of exogenous estrogen and a progesterone analogue (P) on serum lipids and aortic plaque load. Serum cholesterol (C) and triglyceride (T) levels and atherosclerotic plaque loads were compared in 5 groups of male New Zealand White rabbits fed a 12-week, C-rich diet: 1 control group (CG) and 4 groups treated with estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the LDP and HDP groups. Serial histologic sections (15 each of 27 ascending aortas) were studied by light microscopy and computerized morphometric analysis. Plaque load is defined as the ratio of intimal area to medial area (I/M). Exogenous E (p<0.001), H (P = 0.02), LDP and HDP (P<0.001), each) were found to be significantly associated with less aortic plaque load than controls. In a multivariate analysis, after controlling for the differences in serum C and T levels, HDP (p = 0.014) was found to be associated with less aortic plaque load than controls, and this association approached statistical significance in the E (p = 0.052) and H (p = 0.069) groups. These data suggest that the mechanism(s) involved with the antiatherogenic effect of HDP in this animal model is, or are, independent of an alteration in serum lipids. AB . . . New Zealand White rabbits fed a 12-week, C-rich diet: 1 control group (CG) and 4 groups treated with estriol (E), haloperidol (H), low-dose 17-hydroxyprogesterone (LDP), or high-dose 17-hydroxyprogesterone (HDP). Serum P was measured in the LDP and HDP groups. Serial histologic sections (15 each of 27 ascending aortas). . . Check Tags: Animal; Male \*17-Hydroxyprogesterone: AD, administration dosage Aorta: DE, drug effects \*Aorta: ME, metabolism Aorta: PA, pathology \*Cholesterol: BL, blood Cholesterol, Dietary: AD, . . ET, etiology \*Coronary Arteriosclerosis: ME, metabolism Coronary Arteriosclerosis: PA, pathology \*Diet, Atherogenic Dose-Response Relationship, Drug Estriol: AD, administration dosage Haloperidol: AD, administration dosage \*Hypercholesterolemia: BL, blood Hypercholesterolemia: ET, etiology Hypercholesterolemia: PA, pathology Image Processing, Computer-Assisted Rabbits \*Triglycerides: BL,. 50-27-1 (Estriol); **52-86-8 (Haloperidol)**; 57-88-5 (Cholesterol); 68-96-2 (17-Hydroxyprogesterone) L13 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2001 ACS Full-text ACCESSION NUMBER: 2000:537881 CAPLUS DOCUMENT NUMBER: 133:246811 TITLE: GRid-INdependent Descriptors (GRIND): A Novel Class of

Alignment-Independent Three-Dimensional Molecular
Descriptors
AUTHOR(S): Pastor, Manuel; Cruciani, Gabriele; McLay, Iain;
Pickett, Stephen; Clementi, Sergio

CORPORATE SOURCE: Laboratory on Chemometrics Department of Chemistry, University of Perugia, Perugia, 06123, Italy

SOURCE: J. Med. Chem. (2000), 43(17), 3233-3243

CODEN: JMCMAR; ISSN: 0022-2623
American Chemical Society

PUBLISHER: American
DOCUMENT TYPE: Journal
LANGUAGE: English

Traditional methods for performing 3D-QSAR rely upon an alignment step that is often time-consuming and can introduce user bias, the resultant model being dependent upon and sensitive to the alignment used. There are several methods which overcome this problem, but in general the necessary transformations prevent a simple interpretation of the resultant models in the original descriptor space (i.e. 3D mol. coordinates). Here we present a novel class of mol. descriptors which we have termed GRid-INdependent Descriptors (GRIND). They are derived in such a way as to be highly relevant for describing biol. properties of compds. while being alignment-independent, chem. interpretable, and easy to compute. GRIND are obtained starting from a set of mol. interaction fields, computed by the program GRID or by other programs. The procedure for computing the descriptors involves a first step, in which the fields are simplified, and a second step, in which the results are encoded into alignment-independent variables using a particular type of autocorrelation transform. The mol. descriptors so obtained can be used to obtain graphical diagrams called "correlograms" and can be used in different chemometric analyses, such as principal component anal. or partial least-squares. An important feature of GRIND is that, with the use of appropriate software, the original descriptors (mol. interaction fields) can be regenerated from the autocorrelation transform and, thus, the results of the anal. represented graphically, together with the original mol. structures, in 3D plots. In this respect, the article introduces the program ALMOND, a software package developed in our group for the computation, anal., and interpretation of GRIND. The use of the methodol. is illustrated using some examples from the field of 3D-QSAR. Highly predictive and interpretable models are obtained showing the promising potential of the novel descriptors in drug design.

REFERENCE COUNT:

REFERENCE(S):

23

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- (3) Baroni, M; Quant Struct-Act Relat 1993, V12, P9 CAPLUS
- (4) Broto, P; Eur J Med Chem 1984, V19, P66 CAPLUS
- (5) Broto, P; Eur J Med Chem 1984, V19, P79 CAPLUS
- (6) Clementi, M; Molecular Modelling and Prediction of Bioreactivity 2000, P207 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

50-03-3, Cortisol-21-acetate 50-22-6, Corticosterone 50-23-7, Cortisol 50-24-8, Prednisolone 50-27-1, Estriol 50-28-2, Estradiol, biological studies 50-99-7D, Glucose, analogs 52-39-1, Aldosterone 52-86-8, Haloperidol 53-06-5, Cortisone 53-16-7, Estrone, biological studies 53-41-8, Androsterone 53-42-9, Etiocholanolone 53-43-0, Dehydroepiandrosterone 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 63-05-8, Androstenedione 64-85-7, Deoxycorticosterone 68-96-2, 17-

Dihydrotestosterone 571-20-0 595-77-7 600-67-9, Epicorticosterone

```
1239-79-8, 16α-Methyl-4-pregnene-3,20-dione 3836-17-7
                                                              33204-32-9
     57039-38-0
                 58825-13-1 133496-57-8 133496-58-9 133496-60-3
     137041-95-3
                  149247-08-5 149247-09-6 149247-10-9 149247-11-0
     149247-12-1 149247-14-3 156209-97-1 165035-30-3 171923-83-4
     187330-53-6 187330-57-0 210702-20-8 210702-21-9 210702-25-3
     211509-10-3 240404-01-7 240404-03-9 240404-08-4
                                                             240404-09-5
     240404-11-9 240404-12-0
                                 240404-13-1
                                              240404-14-2
                                                             295803-27-9
     295803-28-0
                  295803-29-1 295803-30-4
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (GRid-Independent Descriptors (GRIND): novel class of
        alignment-independent three-dimensional mol. descriptors)
L13 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2001 ACS
Full-text
ACCESSION NUMBER:
                         1998:489534 CAPLUS
DOCUMENT NUMBER:
                         129:293760
TITLE:
                         Percutaneous absorption of one hundred drugs and the
                         derivation of an experimental regression equation
AUTHOR (S):
                         Xu, Jingfeng; Zhao, Weijuan; Zhang, Mei; Liu, Mei;
                         Wang, Jinping; Jin, Yinghua; Wang, Yurong
CORPORATE SOURCE:
                         Beijing Military Command Clinical Pharmaceutical
                         Institute, Beijing, 100700, Peop. Rep. China
                         Zhongguo Yaoxue Zazhi (Beijing) (1998), 33(2), 86-91
SOURCE:
                         CODEN: ZYZAEU; ISSN: 1001-2494
PUBLISHER:
                         Zhongquo Yaoxuehui
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         Chinese
    The pharmaceutical regularity of percutaneous absorption was studied. The
     percutaneous absorption speed of 100 drugs and the comparison with the
     permeation enhancer of 2% and 5% Azone were studied in mouse with an
     improved Fick's diffusion installation by computing accumulative
     permeation quantity (Q), steady percutaneous speed (J), and permeation
     coeff. (Kp). The rules in pharmaceutics of drug's phys. and chem.
     characteristics and percutaneous absorption were discussed, and the exptl.
     regression equation of drug percutaneous absorption were calcd. and the
     influence of different concns. of azone on drug percutaneous permeation
    and equation were studied.
    50-14-6, Vitamin D2 50-23-7, Hydrocortisone 50-24-8, Prednisolone
     50-50-0, Estradiol benzoate 50-53-3, Chlorpromazine, biological studies
     50-55-5, Reserpine 50-76-0, Dactinomycin 50-78-2, Aspirin 50-81-7,
     Vitamin C, biological studies 51-21-8, Fluorouracil 51-34-3,
                 51-43-4, Adrenaline 51-61-6, Dopamine, biological studies
     Scopolamine
     52-53-9, Verapamil 52-86-8, Haloperidol 53-21-4,
     Cocaine hydrochloride 54-31-9, Furosemide 54-85-3, Isoniazid
     55-48-1, Atropine sulfate 56-53-1, Diethylstilbestrol 56-95-1,
     Chlorhexidine acetate 57-13-6, Urea, biological studies 57-42-1,
     Pethidine 57-83-0, Progesterone, biological studies 57-85-2,
     Testosterone Propionate 57-92-1, Streptomycin, biological studies
     58-08-2, Caffeine, biological studies 58-15-1, Aminopyrine 58-27-5,
    Vitamin K3
                 58-33-3, Promethazine hydrochloride
                                                       58-74-2, Papaverine
     59-26-7, Nikethamide 59-43-8, Vitamin B1, biological studies 59-46-1,
     Procaine 59-67-6, Nicotinic acid, biological studies 59-98-3,
     Tolazoline 59-99-4, Neostigmine 60-56-0, Methimazole
     Phenacetin 64-65-3, Bemegride 65-85-0, Benzoic acid, biological
             68-19-9, Vitamin B12 68-35-9, Sulfadiazine 68-96-2,
    Hydroxyprogesterone 69-57-8, Benzylpenicillin sodium 69-74-9,
     Cytarabine hydrochloride 77-09-8, Phenolphthalein 83-88-5, Vitamin B2,
    biological studies 85-61-0, Coenzyme A, biological studies 96 Lobeline 94-63-3, Pralidoxime iodide 100-92-5, Mephentermine 100-97-0, biological studies 103-90-2, Paracetamol 110-44-1,
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acid 113-45-1, Methylphenidate 113-92-8 118-55-8, Salol

110-44-1, Sorbic

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135-19-3, Betanaphthol, biological studies 137-58-6, Lidocaine
147-24-0, Diphenhydramine hydrochloride 148-24-3, 8 Hydroxyquinoline,
biological studies 148-72-1, Pilocarpine nitrate 299-42-3, Ephedrine
303-98-0, Coenzyme Q10 317-34-0, Aminophylline 357-70-0, Galanthamine
439-14-5, Diazepam 443-48-1, Metronidazole 479-18-5, Diprophylline
633-65-8, Berberine hydrochloride 723-46-6, Sulfamethoxazol 738-70-5,
              865-21-4, Vinblastine 987-78-0, Citicoline
Trimethoprim
                                                          1124-11-4,
Ligustrazine 1321-11-5, Aminobenzoic acid 1404-00-8, Mitomycin
1837-57-6, Acrinol 2624-44-4, Etamsylate 6961-46-2, Idrocilamide
7683-59-2, Isoprenaline 8059-24-3, Vitamin B6 11104-38-4, Vitamin K1
13292-46-1, Rifampicin 17598-65-1, Deslanoside
                                               26833-87-4,
Homoharringtonine
                 38194-50-2, Sulindac 38821-53-3, Cefradine
51481-61-9, Cimetidine 55869-99-3, Anisodamine 56796-20-4, Cefmetazole
59703-84-3, Piperacillin sodium 68401-81-0, Ceftizoxime 85721-33-1,
Ciprofloxacin
RL: BPR (Biological process); PEP (Physical, engineering or chemical
process); PRP (Properties); BIOL (Biological study); PROC (Process)
   (percutaneous absorption of one hundred drugs and the derivation of an
   exptl. regression equation)
```

# L13 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2001 ACS

### Full-text

ACCESSION NUMBER: 1996:181570 CAPLUS

DOCUMENT NUMBER: 124:233011

TITLE: Preparation of glycoside prodrugs with enhanced water

solubility.

INVENTOR(S): Klemke, R.-Erich; Koreeda, Masato; Houston, Todd A.;

Shull, Brian K.; Tuinman, Roeland J.

PATENT ASSIGNEE(S): Harrier, Inc., USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

GΙ

Patent English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

F	PATENT NO.				KII	KIND DATE APPLICATION NO. DATE														
- V	WO 9532981			A1 19951207				WO 1995-US7027 19950601												
		W:	AM,	AU,	BB,	BG,	BR,	BY,	CA,	CN,	CZ,	EE,	FI,	GE,	HU,	JP,	ΚE,	KG,		
			ΚP,	KR,	ΚZ,	LK,	LR,	LT,	LV,	MD,	MG,	MN,	MW,	MX,	NO,	ΝZ,	PL,	RO,		
			RU,	SD,	SI,	SK,	TJ,	TT,	UA,	UZ,	VN									
*		RW:	ΚE,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,		
			LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML,	MR,	NE,		
			SN,	TD,	TG															
τ	JS	56937	767		A		1997	1202		Ü	S 19	94-2	5186	9	1994	0601				
		95266																		
PRIORI	ITY	APPI	LN.	INFO.	. :				τ	US 1	994-	2518	69	Α	1994	0601				
									τ	US 1	991-	6440	02	A2	1991	0122				
									τ	US 1	991-	7339:	15	B2	1991	0722				
*									Ţ	US 1	992-	8156	91	B2	1992	0124				
									Ţ	US 1	993-	6447		B2	1993	0121				
									7	WO 1	995-1	US70:	27	W	1995	0601				

<sup>\*</sup> STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Glycosides of aliph., alicyclic, aliph.-arom., and arom. aglycons having primary, secondary, or tertiary OH, SH, or CO2H groups with

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2,3-dideoxy-\alpha-D-erythrohex-2-enopyranoside fragments Q1-Q6 (A =
acyl; X = 0, S, CO2), were prepd. Thus, a mixt. of 4-acetamidophenol and
hexaacetyl D-maltal was refluxed with iodine in THF for 12 h to give 30%
of an \alpha,\beta-glycoside, which was stirred with Ba(OH)2 in MeOH to
give glycoside (I). I had 8 times the H2O soly. of tylenol itself in
phosphate-buffered saline at pH 7.4.
50-02-2DP, Dexamethasone, dideoxyhexenopyranoside glycoside deriv.
50-22-6DP, Corticosterone, dideoxyhexenopyranoside glycoside deriv.
50-23-7DP, Cortisol, dideoxyhexenopyranoside glycoside deriv.
dideoxyhexenopyranoside glycoside deriv. 50-28-2DP, 17β-Estradiol,
dideoxyhexenopyranoside glycoside deriv. 50-81-7DP, Ascorbic acid,
dideoxyhexenopyranoside glycoside deriv. 51-34-3DP,
dideoxyhexenopyranoside glycoside deriv.
                                           51-55-8DP, Atropine,
dideoxyhexenopyranoside glycoside deriv. 52-86-8DP,
Haloperidol, ditleoxyhexenopyranoside glycoside deriv.
Urocortisol, dideoxyhexenopyranoside glycoside deriv.
                                                        53-06-5DP,
Cortisone, dideoxyhexenopyranoside glycoside deriv. 53-16-7DP, Estrone,
dideoxyhexenopyranoside glycoside deriv. 53-41-8DP, Androsterone,
dideoxyhexenopyranoside glycoside deriv. 56-75-7DP, Chloramphenicol,
dideoxyhexenopyranoside glycoside deriv. 57-62-5DP, Chlortetracycline,
dideoxyhexenopyranoside glycoside deriv. 57-63-6DP, Ethinylestradiol,
dideoxyhexenopyranoside glycoside deriv. 58-22-0DP, Testosterone,
dideoxyhexenopyranoside glycoside deriv. 58-39-9DP, Perphenazine,
dideoxyhexenopyranoside glycoside deriv. 59-42-7DP, Phenylephrine, dideoxyhexenopyranoside glycoside deriv. 59-43-8DP, Thiamin,
dideoxyhexenopyranoside glycoside deriv.
                                           59-47-2DP, Mephenesin,
dideoxyhexenopyranoside glycoside deriv.
                                           59-61-0DP.
Dichloroisoproterenol, dideoxyhexenopyranoside glycoside deriv.
59-92-7DP, Levodopa, dideoxyhexenopyranoside glycoside deriv.
                                                                60-54-8DP,
Tetracycline, dideoxyhexenopyranoside glycoside deriv.
                                                         60-79-7DP,
Ergonovine, dideoxyhexenopyranoside glycoside deriv. 64-85-7DP,
11-Desoxycorticosterone, dideoxyhexenopyranoside glycoside deriv.
66-81-9DP, Cycloheximide, dideoxyhexenopyranoside glycoside deriv.
68-42-8DP, Tetrahydrocorticosterone, dideoxyhexenopyranoside glycoside
       68-88-2DP, Hydroxyzine, dideoxyhexenopyranoside glycoside deriv.
68-96-2DP, 17\alpha-Hydroxyprogesterone, dideoxyhexenopyranoside
glycoside deriv. 69-23-8DP, Fluphenazine, dideoxyhexenopyranoside
glycoside deriv. 72-33-3DP, Mestranol, dideoxyhexenopyranoside glycoside
        79-57-2DP, Oxytetracycline, dideoxyhexenopyranoside glycoside
deriv.
         81-25-4DP, Cholic acid, dideoxyhexenopyranoside glycoside deriv.
83-44-3DP, Deoxycholic acid, dideoxyhexenopyranoside glycoside deriv.
87-00-3DP, Homatropine, dideoxyhexenopyranoside glycoside deriv.
90-33-5DP, Hymecromone, dideoxyhexenopyranoside glycoside deriv.
93-14-1DP, Guaiacol glycerol ether, dideoxyhexenopyranoside glycoside
        103-90-2DP, Acetaminophen, dideoxyhexenopyranoside glycoside
         104-14-3DP, p-Hydroxyphenylethanolamine, dideoxyhexenopyranoside
glycoside deriv. 127-40-2DP, Xanthophyll, dideoxyhexenopyranoside
glycoside deriv. 129-20-4DP, Oxyphenbutazone, dideoxyhexenopyranoside
glycoside deriv. 145-13-1DP, Pregnenolone, dideoxyhexenopyranoside
glycoside deriv. 152-43-2DP, Quinestrol, dideoxyhexenopyranoside
glycoside deriv. 152-58-9DP, 11-Desoxycortisol, dideoxyhexenopyranoside
                  299-42-3DP, Ephedrine, dideoxyhexenopyranoside
glycoside deriv.
glycoside deriv. 387-79-1DP, 17\alpha-Hydroxypregnenolone,
dideoxyhexenopyranoside glycoside deriv. 404-86-4DP, Capsaicin,
dideoxyhexenopyranoside glycoside deriv. 447-41-6DP, Buphenine,
dideoxyhexenopyranoside glycoside deriv. 474-25-9DP, Chenodeoxycholic
acid, dideoxyhekenopyranoside glycoside deriv. 536-21-0DP, Norfenefrine,
dideoxyhexenopyranoside glycoside deriv. 551-11-1DP, Prostaglandin
F2α, dideoxyhexenopyranoside glycoside deriv. 555-30-6DP,
Methyldopa, dideoxyhexenopyranoside glycoside deriv. 586-06-1DP,
Metaproterenol, dideoxyhexenopyranoside glycoside deriv. 640-85-7DP,
Allocortolone, dideoxyhexenopyranoside glycoside deriv. 673-31-4DP,
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Phenprobamate, dideoxyhexenopyranoside glycoside deriv.
                                                               709-55-7DP,
     Etilefrin, dideoxyhexenopyranoside glycoside deriv.
                                                           749-13-3DP,
     Trifluperidol, dideoxyhexenopyranoside glycoside deriv.
                                                               1050-79-9DP,
     Moperone, dideoxyhexenopyranoside glycoside deriv.
                                                         1406-18-4DP, Vitamin
     E, dideoxyhexentpyranoside glycoside deriv.
                                                   2470-73-7DP, Dixyrazine,
     dideoxyhexenopyranoside glycoside deriv. 2622-26-6DP, Pericyazine,
     dideoxyhexenopyranoside glycoside deriv. 2751-68-0DP, Acetophenazine,
     dideoxyhexenopyranoside glycoside deriv.
                                               4419-39-ODP, Beclomethasone,
     dideoxyhexenopyranoside glycoside deriv.
                                                7683-59-2DP, Isoprenaline,
     dideoxyhexenopyranoside glycoside deriv.
                                                9061-77-2DP, Provitamin D,
     dideoxyhexenopyranoside glycoside deriv.
                                               11029-02-0DP, Dolichol,
     dideoxyhexenopyranoside glycoside deriv.
                                               11103-57-4DP, Vitamin A,
     dideoxyhexenopyranoside glycoside deriv.
                                               14860-49-2DP, Clobutinol,
     dideoxyhexenopyranoside glycoside deriv.
                                               15318-45-3DP, Thiamphenicol,
     dideoxyhexenopyranoside glycoside deriv.
                                                16589-24-5DP,
     dideoxyhexenopyranoside glycoside deriv.
                                                20830-81-3DP, Daunorubicin,
     dideoxyhexenopyranoside glycoside deriv.
                                                21343-40-8DP,
     25-Hydroxycalciferol, dideoxyhexenopyranoside glycoside deriv.
     23031-25-6DP, Terbutaline, dideoxyhexenopyranoside glycoside deriv.
     23339-28-8P
                 23651-95-8DP, Droxidopa, dideoxyhexenopyranoside glycoside
              26787-78-0DP, Amoxicillin, dideoxyhexenopyranoside glycoside
              28860-95-9DP, Carbidopa, dideoxyhexenopyranoside glycoside deriv.
     34758-83-3DP, Zipeprol, dideoxyhexenopyranoside glycoside deriv.
     58001-44-8DP, Clavulanic acid, dideoxyhexenopyranoside glycoside deriv.
     69038-96-6DP, Tropine benzilate, dideoxyhexenopyranoside glycoside deriv.
     73573-88-3DP, Mevastatin, dideoxyhexenopyranoside glycoside deriv.
     75330-75-5DP, Lovastatin, dideoxyhexenopyranoside glycoside deriv.
     79902-63-9DP, Simvastatin, dideoxyhexenopyranoside glycoside deriv.
     136468-12-7P
                   136468-13-8P
                                   136468-14-9P
                                                 149279-28-7P
                                                                 149279-29-8P
     149279-31-2P
                   149279-35-6P
                                   149279-38-9P
                                                  149279-39-0P
                                                                 168072-61-5P
     168072-62-6P
                   174670-06-5P
                                   174670-07-6P
                                                  174670-08-7P
                                                                 174670-09-8P
     174670-10-1P
                   174670-11-2P
                                  174670-12-3P
    RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of glycoside prodrugs with enhanced water soly.)
L13 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2001 ACS
Full-text
ACCESSION NUMBER:
                         1995:211710 CAPLUS
DOCUMENT NUMBER:
                         122:1283
TITLE:
                         Relationship between sigma-like site and
                         progesterone-binding site of adult male rat liver
                         microsomes
AUTHOR (S):
                         Yamada, Morio; Nishigami, Takashi; Nakasho, Keiji;
                         Nishimoto, Yukiyasu; Miyaji, Hideki
                         2nd Department Pathology, Hyogo College Medicine,
CORPORATE SOURCE:
                         Nishinomiya, 663, Japan
SOURCE:
                         Hepatology (St. Louis) (1994), 20(5), 1271-80
                         CODEN: HPTLD9; ISSN: 0270-9139
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
    The authors demonstrated that adult male rat liver microsomes, esp. smooth
     endoplasmic reticulum, possessed a saturable haloperidol-binding site
    closely resembling the \sigma site, with a high affinity (Kd 1.0 nmol/L)
     and high capacity (Bmax 9.3 pmol/mg protein) and with the rank order of
    affinity of the ligands: haloperidol > reduced haloperidol >
    clorgyline > ifenprodil > 1,3-di(2-tolyl)guanidine, (-)-butaclamol >
```

GBR-12909 > SKF-525A > progesterone >  $5\alpha$ -dihydrotestosterone > R(+)-3- (hydroxyphenyl)-N-propylpiperidine > testosterone >>

corticosteroids, estradiol- $17\beta$ , cholesterol and neuroactive compds. displaying high affinities for other neurotransmitter receptors such as

dopamine D2, serotonin (5-HT1A and 5-HT2) and  $\alpha$ 1-adrenergic and GABAA receptors. This rank order showed a high correlation (r = 0.908) with that of a large portion (-85%) of specific progesterone-binding site (Kd 31.0 nmol/L, Bmax 5.7 pmol/mg protein) of the same source. Therefore, these two sites were suggested to be the same or closely related. Furthermore, the authors provide a strong suggestion that these sites are neither identical with some subforms of the microsomal cytochromes P 450 or other steroid/drug-metabolizing enzymes nor participate universally and directly in the progesterone metabolizing processes.

AΒ The authors demonstrated that adult male rat liver microsomes, esp. smooth endoplasmic reticulum, possessed a saturable haloperidol-binding site closely resembling the  $\sigma$  site, with a high affinity (Kd 1.0 nmol/L) and high capacity (Bmax 9.3 pmol/mg protein) and with the rank order of affinity of the ligands: haloperidol > reduced haloperidol > clorgyline > ifenprodil > 1,3-di(2-tolyl)guanidine, (-)-butaclamol > GBR-12909 > SKF-525A > progesterone >  $5\alpha$ -dihydrotestosterone > R(+)-3- (hydroxyphenyl)-N-propylpiperidine > testosterone >> corticosteroids, estradiol-17 $\beta$ , cholesterol and neuroactive compds. displaying high affinities for other neurotransmitter receptors such as dopamine D2, serotonin (5-HT1A and 5-HT2) and  $\alpha$ 1-adrenergic and GABAA receptors. This rank order showed a high correlation (r = 0.908) with that of a large portion (~85%) of specific progesterone-binding site (Kd 31.0 nmol/L, Bmax 5.7 pmol/mg protein) of the same source. Therefore, these two sites were suggested to be the same or closely related. Furthermore, the authors provide a strong suggestion that these sites are neither identical with some subforms of the microsomal cytochromes P 450 or other steroid/drug-metabolizing enzymes nor participate universally and directly in the progesterone metabolizing processes.

# IT 52-86-8, Haloperidol

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

(sigma-like site and progesterone-binding site of liver microsomes)

IT 68-96-2,  $17\alpha$ -Hydroxyprogesterone 145-14-2,

20 $\alpha$ -Hydroxyprogesterone 438-07-3, 16 $\alpha$ -Hydroxyprogesterone 604-19-3, 6 $\beta$ -Hydroxyprogesterone 604-28-4, 2 $\alpha$ -

Hydroxyprogesterone

RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(sigma-like site and progesterone-binding site of liver microsomes)

# L13 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2001 ACS

## Full-text

ACCESSION NUMBER: 1990:229347 CAPLUS

DOCUMENT NUMBER: 112:229347

TITLE: Neuroendocrinological effects of ketoconazole in rats

AUTHOR(S): Irsy, Gabor; Koranyi, Lajos

CORPORATE SOURCE: 1st Dep. Med., Postgrad. Med. Sch., Budapest, H-1389,

Hung.

Journal

SOURCE: Acta Endocrinol. (1990), 122(3), 409-13

CODEN: ACENA7; ISSN: 0001-5598

DOCUMENT TYPE:

LANGUAGE: English

The effect of ketoconazole on steroid synthesis was studied in intact (sham-operated) and castrated male and ovariectomized female rats. Rats were given 25 mg/kg ketoconazole twice a day i.m. for 5 days. The influence of ketoconazole was also investigated on hormone release altered by GnRH (LHRH), estradiol and haloperidol. The following hormones were measured: serum LH, prolactin (PRL), testosterone, corticosterone, 17-OH-progesterone, estradiol, and dopamine content of the tubero-infundibular area. Ketoconazole treatment resulted in a

significant decrease of testosterone level, whereas LH, PRL, corticosterone and 17-OH-progesterone remained unchanged in the male rat. The effect of castration on LH level was reduced by ketoconazole in male and female rats, but the GnRH-stimulated LH release in castrated and ovariectomized animals was unchanged. The suppressive action of estradiol on LH in ovariectomized rats was enhanced, and its priming effect on PRL release was diminished by ketoconazole. Ketoconazole failed to modify the tubero-infundibular dopamine content and haloperidol-induced PRL release. It can be assumed that in addn. to its inhibitory role of steroid biosynthesis ketoconazole has an influence on central mechanisms underlying LH and PRL release.

The effect of ketoconazole on steroid synthesis was studied in intact (sham-operated) and castrated male and ovariectomized female rats. Rats were given 25 mg/kg ketoconazole twice a day i.m. for 5 days. The influence of ketoconazole was also investigated on hormone release altered by  ${\tt GnRH}$  (LHRH), estradiol and  ${\tt haloperidol}.$  The following hormones were measured: serum LH, prolactin (PRL), testosterone, corticosterone, 17-OH-progesterone, estradiol, and dopamine content of the tubero-infundibular area. Ketoconazole treatment resulted in a significant decrease of testosterone level, whereas LH, PRL, corticosterone and 17-OH-progesterone remained unchanged in the male rat. The effect of castration on LH level was reduced by ketoconazole in male and female rats, but the GnRH-stimulated LH release in castrated and ovariectomized animals was unchanged. The suppressive action of estradiol on LH in ovariectomized rats was enhanced, and its priming effect on PRL release was diminished by ketoconazole. Ketoconazole failed to modify the tubero-infundibular dopamine content and haloperidol-induced PRL release. It can be assumed that in addn. to its inhibitory role of steroid biosynthesis ketoconazole has an influence on central mechanisms underlying LH and PRL release.

## IT 52-86-8

RL: BIOL (Biological study)

(prolactin release stimulation by, ketoconazole effect on) 50-22-6, Corticosterone 50-28-2, Estradiol, biological studies 58-22-0, Testosterone 68-96-2, 17-

Hydroxyprogesterone 9002-62-4, Prolactin, biological studies 9002-67-9, LH

RL: BIOL (Biological study)

(release of, ketoconazole effect on, neuroendocrine system in)

# L13 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2001 ACS

# Full-text

ACCESSION NUMBER: 1989:87907 CAPLUS

DOCUMENT NUMBER: 110:87907

TITLE:

Xenobiotic and endobiotic inhibitors of cytochrome

P-450dbl function, the target of the debrisoquine/sparteine type polymorphism Fonne-Pfister, Raymonde; Meyer, Urs A.

AUTHOR (S): CORPORATE SOURCE:

Biocent., Univ. Basel, Basel, CH-4056, Switz.

SOURCE: Biochem. Pharmacol. (1988), 37(20), 3829-35

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE:

LANGUAGE:

Journal English

Five to 10% of Caucasians are poor metabolizers of debrisoquine, sparteine, bufuralol, and numerous other drugs. A deficiency in cytochrome P-450dbl (P-450dbl) function is the cause of this polymorphism of drug oxidn., which has autosomal recessive inheritance. In the present study, inhibition of bufuralol-1'-hydroxylase in human liver microsomes by drugs and other chems. was tested in a search for potential new substrates for this polymorphic enzyme. Of the 80 alkaloids and drugs tested, 25 were competitive inhibitors. In vitro competitive inhibition of bufuralol oxidn. by a substance indicates that this compd. is able to bind to the

```
same enzymic site as bufuralol. This may mean that the competing drug
     also is metabolized by P-450dbl and that its metab. is subject to the same
     genetic variation as the oxidn. of bufuralol. However, some of these
     competitive inhibitors are not oxidized by P-450dbl. In this case,
     however, they may interfere with the in vivo phenotyping procedure by .
     inhibiting the formation of metabolites of test drugs such as
     debrisoquine, sparteine, metoprolol, or dextromethorphan.
IT
     50-27-1, Estriol 50-28-2, \beta-Estradiol, biological studies
     50-55-5, Reserpine 50-67-9, Serotonin, biological studies
     Norepinephrine 51-43-4, Epinephrine 51-61-6, Dopamine, biological
     studies 51-71-8, Phenelzine
                                    51-98-9 52-86-8,
     Haloperidol 53-16-7, Estrone, biological studies
                                                           57-22-7,
     Vincristine
                  57-83-0, Pregn-4-ene-3,20-dione, biological studies
     57-88-5, Cholesterol, biological studies 58-00-4, Apomorphine 58-73-1
     59-92-7, L-Dopa, biological studies 61-54-1, Tryptamine 63-05-8,
     Androst-4-ene-3,17-dione 68-96-2 69-23-8, Fluphenazine
     71-63-6, Digitoxin 73-31-4, Melatonin 83-74-9, Ibogaine 87-52-5,
     Gramine 90-69-7, \alpha-Lobeline 97-31-4, Normetanephrine 104-14-3,
     Octopamine 113-15-5, Ergotamine 304-21-2, Harmaline 364-62-5,
     Metoclopramide 445-30-7, Homarine 458-88-8, Coniine 483-04-5,
     Ajmalicine 500-44-7, Mimosine 509-15-9, Gelsemine 548-73-2,
     Droperidol
                 549-92-8, Sempervirine 555-57-7, Pargyline 749-02-0,
                749-13-3, Trifluperidol 865-21-4, Vinblastine 1617-90-9,
     Spiperone
     Vincamine 2062-84-2, Benperidol 2086-83-1, Berberine 2688-77-9,
     Laudanosine 3737-09-5, Disopyramide 4360-12-7, Ajmaline
                                                                   5001-33-2,
     Metanephrine 5233-54-5 5796-17-8, D-Dopa 10338-69-9,
     4-Phenyl-1,2,3,6-tetrahydropyridine 13074-31-2, Tetrahydropapaverine
     15676-16-1, Sulpiride 16589-24-5, Synephrine 25614-03-3, Bromocriptine 27740-96-1, Salsolinol 28289-54-5, MPTP 31309-39-4, Medipine
     31314-38-2, Prodipine 34273-01-3, 4,4-Diphenylpiperidine 34535-98-3, Phenylcyclopropylamine 36913-39-0, 1-Methyl-4-phenylpyridinium iodide
     55985-32-5, Nicardipine 57808-66-9, Domperidone 57982-78-2, Budipine
     97467-07-7 118956-95-9
     RL: BIOL (Biological study)
        (bufuralol hydroxylase of human liver microsome inhibition by, genetics
        in relation to)
L13 ANSWER 8 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
Full-text
ACCESSION NUMBER:
                    2000360597 EMBASE
TITLE:
                    [Secondary amenorrhoea].
                    AMENORRHEE SECONDAIRE.
AUTHOR:
                    Levy D.; Gompel A.
CORPORATE SOURCE:
                    Dr. D. Levy, Service de Gynecologie, L'Hotel Dieu, 75181
                    Paris Cedex 04, France
SOURCE:
                    Revue du Praticien, (1 Oct 2000) 50/15 (1709-1713).
                    ISSN: 0035-2640 CODEN: REPRA3
COUNTRY:
                    France
DOCUMENT TYPE:
                    Journal; General Review
FILE SEGMENT:
                    010
                            Obstetrics and Gynecology
                    037
                            Drug Literature Index
                    038
                            Adverse Reactions Titles
LANGUAGE:
                    French
    Medical Descriptors:
     *secondary . . .
     AE, adverse drug reaction
     estrogen: AE, adverse drug reaction
     fluvoxamine malwate: AE, adverse drug reaction
     buflomedil: AE, adverse drug reaction
     triazolam: AE, adverse drug reaction
     haloperidol: AE, adverse drug reaction
```

zopiclone: AE, adverse drug reaction

```
unindexed drug: AE, adverse drug reaction
     (follitropin) 9002-68-0; (luteinizing hormone) 39341-83-8, 9002-67-9;
      (testosterone) 58-22-0; (androstenedione) 26264-53-9, 63-05-8;
      (hydroxyprogesterone) 68-96-2; (gonadorelin) 33515-09-2, 9034-40-6;
      (nifedipine) 21829-25-4; (veralipride) 66644-81-3; (methyldopa) 555-29-3,
     555-30-6; (clomipramine) 17321-77-6, 303-49-1; (hydroxyzine) 2192-20-3,
     64095-02-9, 68-88-2; (ranitidine) 66357-35-5, 66357-59-3;. . .
     (diazepam) 439-14-5; (sulpiride) 15676-16-1; (pethidine) 28097-96-3,
     50-13-5, 57-42-1; (droperidol) 548-73-2; (meprobamate) 57-53-4;
     (fluvoxamine maleate) 61718-82-9; (buflomedil) 35543-24-9, 55837-25-7;
     (triazolam) 28911-01-5; (haloperidol) 52-86-8; (zopiclone) 43200-80-2
     Adalate; Agreal; Aldomet; Anafranil; Atarax; Azantac; Buspar; Colchimax;
     Deroxat; Dolosal; Droleptan; Equanil; Floxyfral; Fonzylane; Halcion;
     Haldol; Imovane
L13 ANSWER 9 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
Full-text
ACCESSION NUMBER:
                    91344255 EMBASE
DOCUMENT NUMBER:
                    1991344255
TITLE:
                    Hair loss in women. Part II: Treatment options.
AUTHOR:
                    Stein Gardner S.; Conte M.A.; McKay M.
CORPORATE SOURCE:
                    Emory University School of Medicine, Atlanta, GA 30322,
                    United States
SOURCE:
                    Female Patient - Practical Ob/Gyn Medicine, (1991) 16/10
                     (37-52).
                    ISSN: 0888-2401 CODEN: FPPME5
COUNTRY:
                    United States
DOCUMENT TYPE:
                    Journal; Article
FILE SEGMENT:
                     003
                            Endocrinology
                    006
                            Internal Medicine
                    010
                            Obstetrics and Gynecology
                    013
                            Dermatology and Venereology
                    024
                            Anesthesiology
                    032
                            Psychiatry
                    037
                            Drug Literature Index
                    038
                            Adverse Reactions Titles
LANGUAGE:
                    English
SUMMARY LANGUAGE:
                    English
     Treatments for alopecia are diverse, depending on the cause. The prognosis
     is good in most cases, but regrowth requires patience and may involve some
     trial and error. The concluding article in this series focuses on therapy
     according to etiology.
     Medical Descriptors:
     *alopecia: .
     reaction
     epiandrosterone: EC, endogenous compound
     estrogen: DT, drug therapy
     etretinate: AE, adverse drug reaction
     follitropin: EC, endogenous compound
     gentamicin: AE, adverse drug reaction
     griseofulvin: DT, drug therapy
     haloperidol: AE, adverse drug reaction
     heparin: AE, adverse drug reaction
     hydrocortisone: EC, endogenous compound
     hydroxyprogesterone: EC, endogenous compound
     indometacin: AE, adverse drug reaction
     isotretinoin: AE, adverse. . .
     . . 53-21-4, 5937-29-1; (cyproterone acetate) 427-51-0; (doxepin)
     1229-29-4, 1668-19-5; (epiandrosterone) 481-29-8; (etretinate) 54350-48-0;
     (follitropin) 9002-68-0; (gentamicin) 1392-48-9, 1403-66-3, 1405-41-0;
     (griseofulvin) 126-07-8; (haloperido1) 52-86-8; (heparin) 37187-54-5,
     8057-48-5, 8065-01-8, 9005-48-5; (hydrocortisone) 50-23-7;
```

(hydroxyprogesterone) 68-96-2; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (isotretinoin) 4759-48-2; (levodopa) 59-92-7; (lithium) 7439-93-2; (luteinizing hormone) 39341-83-8, 9002-67-9; (methysergide) 16509-15-2, 361-37-5, 62288-72-6; (metoprolol) 37350-58-6;.

L13 ANSWER 10 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

Full-text

ACCESSION NUMBER: 81141856 EMBASE

DOCUMENT NUMBER:

1981141856

TITLE: Effects of chronic neuroleptic therapy on human PRL

secretion and testicular function.

AUTHOR: Magrini G.; Gasperi M.; Martin Du Pan R.; et al. CORPORATE SOURCE: Div. Biochim. Clin., Dept. Med., CHUV, 1011 Lausanne,

Switzerland

Archives of Andrology, (1981) 6/3 (219-228). SOURCE:

CODEN: ARANDR

COUNTRY: United States

DOCUMENT TYPE:

Journal

FILE SEGMENT:

Drug Literature Index 037 028 Urology and Nephrology 029 Clinical Biochemistry

032 Psychiatry

003 Endocrinology

LANGUAGE: English

Correlation between secretion of testicular steroids and plasma prolactin (PRL) levels, before and during bromocriptin treatment, was studied in 20 psychiatric patients under neuroleptic therapy for two years or longer. Eleven of them were under additional treatment with antiparkinson drugs (AP group). Plasma PRL, testosterone (T),  $5\alpha$ -dihydrotestosterone (DHT),  $17\beta$ -estradiol (E2),  $17\alpha$  OH-progesterone (17 $\alpha$  OHP), and dehydroepiandrosterone-sulfate (D-S) were measured by specific RIA both at basal level and in response to testicular stimulation by hCG. Mean basal PRL levels were normal in the patients under neuroleptic treatment alone (Ne group), and slightly elevated in the AP group. In the Ne group, an unexpected, significant increase occurred in mean plasma PRL during the hCG stimulation, before bromocriptine treatment. Mean basal steroid levels were normal in both groups. The testicular responses to hCG, as reflected by the T, E2, 19 $\alpha$  OHP, and DHT mean plasma levels, were within the normal ranges in the AP group; in the Ne group, however, T and DHT displayed a subnormal mean increase, while E2 and  $17\alpha$  OHP responses were within the normal range. These results suggest that some modifications of the enzymatic activity for testicular steroidogenesis could be induced in the patients under neuroleptic treatment alone. Moreover, a significant reverse correlation was found between PRL and  $\ensuremath{\mathtt{T}}$ basal levels in both groups; this correlation disappeared during the bromocriptine treatment.

Medical Descriptors:

\*hormone release

\*mental disease

\*steroidogenesis

\*testis

adverse drug reaction hormone blood level drug therapy

endocrine system

therapy

central nervous system major clinical study male genital system

drug blood level

\*hydroxyprogesterone

\*androstanolone

```
*bromocriptine
     *chlorpromazine
     *chlorprothixene
     *clozapine
     *estradiol
     *fluphenazine
     *haloperidol
     *levomepromazine
     *moperone
     *periciazine
     *prasterone sulfate
     *prolactin
     *testosterone
     *thioridazine
     neuroleptic agent
     bromocriptine mesilate
RN
     (hydroxyprogesterone) 68-96-2; (androstanolone) 521-18-6;
     (bromocriptine) 25614-03-3; (chlorpromazine) 50-53-3, 69-09-0;
     (chlorprothixene) 113-59-7, 6469-93-8; (clozapine) 5786-21-0; (estradiol)
     50-28-2; (fluphenazine) 146-56-5, 69-23-8; (haloperidol) 52-86-8;
     (levomepromazine) 1236-99-3, 60-99-1, 7104-38-3; (moperone) 1050-79-9,
     3871-82-7; (periciazine) 2622-26-6; (prasterone sulfate) 651-48-9;
     (prolactin) 12585-34-1, 50647-00-2, 9002-62-4; (testosterone) 58-22-0;
     (thioridazine) 130-61-0,.
L13 ANSWER 11 OF 16 USPATFULL
Full-text
ACCESSION NUMBER:
                        2001:74959 USPATFULL
TITLE:
                        Solubility parameter based drug delivery system and
                        method for altering drug saturation concentration
INVENTOR (S):
                        Miranda, Jesus, Miami, FL, United States
                        Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S):
                        Noven Pharmaceuticals, Inc., Miami, FL, United States
                        (U.S. corporation)
                             NUMBER
                                           DATE
PATENT INFORMATION:
                        US 6235306
                                         20010522
                        US 1999-274886
APPLICATION INFO.:
                                         19990323 (9)
                        Continuation of Ser. No. US 1995-433754, filed on 4 May
RELATED APPLN. INFO.:
                        1995, now patented, Pat. No. US 5958446 Continuation of
                        Ser. No. US 1991-722342, filed on 27 Jun 1991, now
                        patented, Pat. No. US 5474783, issued on 12 Dec 1995
                        Utility
DOCUMENT TYPE:
PRIMARY EXAMINER:
                        Harrison, Robert H.
LEGAL REPRESENTATIVE:
                        Foley Lardner
NUMBER OF CLAIMS:
                        1
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS: 5
                        15 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT:
                        1306
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The method of adjusting the saturation concentration of a drug in a
       transdermal composition for application to the dermis, which comprises
       mixing polymers having differing solubility parameters, so as to
       modulate the delivery of the drug. This results in the ability to
       achieve a predetermined permeation rate of the drug into and through the
       dermis. In one embodiment, a dermal composition of the present invention
       comprises a drug, an acrylate polymer, and a polysiloxane. The dermal
       compositions can be produced by a variety of methods known in the
       preparation of drug-containing adhesive preparations, including the
       mixing of the polymers, drug, and additional ingredients in solution,
       followed by removal of the processing solvents. The method and
```

composition of this invention permit selectable loading of the drug into the dermal formulation and adjustment of the delivery rate of the drug from the composition through the dermis, while maintaining acceptable shear, tack, and peel adhesive properties.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . nitroglycerin. In still other embodiments, the bioactive agent is a cholinergic agent, such as pilocarpine, or an antipsychotic such as haloperidol or a tranquilizer/sedative such as alprazolam.

DETD . . . action on the central nervous system, for example sedatives, hyponotics, antianxiety agents, analgesics and anesthetics, such as, chloral, buprenorphine, naloxone, haloperidol, fluphenazine, pentobarbital, phenobarbital, secobarbital, codeine, lidocaine, tetracaine, dyclonine, dibucaine, cocaine, procaine, mepivacaine, bupivacaine, etidocaine, prilocaine, benzocaine, fentanyl, and nicotine.

DETD 25. Antipsychotics such as thiopropazate, chlorpromazine, triflupromazine, mesoridazine, piperacetazine, thioridazine, acetophenazine, fluphenazine, perphenazine, trifluoperazine, chlorprathixene, thiothixene, haloperidol, bromperidol, loxapine, and molindone.

ΙT 50-27-1, Estriol 50-28-2,  $17\beta$ -Estradiol, biological studies 50-36-2, Cocaine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 50-54-4, Quinidine sulfate 51-06-9, Procainamide 51-83-2, Carbachol 51-84-3, Acetylcholine, biological studies 51-98-9, Norethindrone acetate 52-53-9, Verapamil 52-86-8, Haloperidol 53-16-7, Estrone, biological studies 54-11-5, Nicotine 55-63-0, Nitroglycerin 55-92-5, Methacholine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol 57-83-0, Progesterone, biological studies 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-94-6, Chlorothiazide 59-46-1, Procaine 62-49-7, Choline 63-75-2, Arecoline 68-22-4, Norethindrone 68-23-5, Norethynodrel 68-96-2, 17-Hydroxyprogesterone 69-23-8, Fluphenazine 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 73-48-3, Bendroflumethiazide 76-57-3, Codeine 79-64-1, Dimethisterone 84-06-0, Thiopropazate 85-79-0, Dibucaine 87-33-2, Isosorbide dinitrate 92-13-7, Pilocarpine 94-09-7, Benzocaine 96-88-8, Mepivacaine 113-59-7 117-89-5, Trifluoperazine Tetracaine 137-58-6, Lidocaine 146-54-3, Triflupromazine 152-62-5, Dydrogesterone 297-76-7, Ethynodiol diacetate 300-54-9, Muscarine 434-03-7, Ethisterone 437-38-7, Fentanyl 439-14-5, Diazepam 472-54-8, 19-Norprogesterone 474-86-2, Equilin 525-66-6, Propranolol 586-06-1, Metaproterenol 586-60-7, Dyclonine 595-33-5, Megestrol acetate 604-75-1, Oxazepam 630-56-8 721-50-6, Prilocaine 846-49-1, Lorazepam 1622-61-3, Clonazepam 1961-77-9, Chlormadinone 1977-10-2, Loxapine 2180-92-9, Bupivacaine 2751-68-0, Acetophenazine 2955-38-6, Prazepam 3819-00-9, Piperacetazine 4205-90-7, Clonidine 5588-33-0, Mesoridazine 5591-45-7, Thiothixene 5633-18-1, Melengestrol 6533-00-2, Norgestrel 7280-37-7, Estropipate 7416-34-4, Molindone 10116-22-0, Demegestone 10457-90-6, Bromperidol 13392-18-2, Fenoterol 13642-52-9, Soterenol 13757-97-6, Quinterenol 16051-77-7, Isosorbide mononitrate 17617-23-1, Flurazepam 18559-94-9, Albuterol 18910-65-1, Salmefamol 19216-56-9, Prazosin 21829-25-4, Nifedipine 23031-25-6, Terbutaline 23092-17-3, Halazepam 23887-31-2 26839-75-8, Timolol 28911-01-5, Triazolam 28981-97-7, Alprazolam 30418-38-3, Tretoquinol 32953-89-2, Rimiterol 34184-77-5, Promegestone 34866-47-2, Carbuterol 36637-18-0, Etidocaine 42399-41-7, Diltiazem 52485-79-7, Buprenorphine 55985-32-5, Nicardipine 62571-86-2, Captopril 91609-06-2, Betanechol (transdermal pressure-sensitive adhesive delivery system for, controlled-release)

Full-text ACCESSION NUMBER: 2001:59406 USPATFULL Solubility parameter based drug delivery system and method for altering drug saturation concentration INVENTOR (S): Miranda, Jesus, Miami, FL, United States Sablotsky, Steven, Miami, FL, United States PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation) NUMBER DATE -----PATENT INFORMATION: US 6221383 20010424 APPLICATION INFO .: US 1999-318121 19990525 (9) RELATED APPLN. INFO.: Division of Ser. No. US 1997-907906, filed on 11 Aug 1997 Continuation-in-part of Ser. No. US 1994-178558, filed on 7 Jan 1994, now patented, Pat. No. US 5656286, issued on 12 Aug 1997 DOCUMENT TYPE: Utility PRIMARY EXAMINER: Dodson, Shelley A. ASSISTANT EXAMINER: Williamson, Michael A. LEGAL REPRESENTATIVE: Foley Lardner NUMBER OF CLAIMS: 4 EXEMPLARY CLAIM: 1 NUMBER OF DRAWINGS: 20 Drawing Figure(s); 19 Drawing Page(s) LINE COUNT: CAS INDEXING IS AVAILABLE FOR THIS PATENT. A blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug provides a pressure-sensitive adhesive composition for a transdermal drug delivery system in which the drug is delivered from the pressure-sensitive adhesive composition and through dermis when the pressure-sensitive adhesive composition is in contact with human skin. According to the invention, soluble polyvinylpyrrolidone can be used to prevent crystallization of the drug, without affecting the rate of drug delivery from the pressure-sensitive adhesive composition. CAS INDEXING IS AVAILABLE FOR THIS PATENT. . . . as nitroglycerin. In still other embodiments, the drug is a cholinergic agent, such as pilocarpine, or an antipsychotic such as haloperidol or a tranquilizer/sedative such as alprazolam. Butyrophenones such as Benperidol, Bromperidol, Droperidol, Fluanisone, Haloperidol, Melperone, Moperone, Pipamperone, Sniperone, Timiperone and Trifluperidol; . . . substantially crystal-free. Other specific drugs for which DETD soluble PVP is particularly usefully employed according to the invention include albuterol, estradiol, haloperidol and alprazolam. DETD . . Adhesive 56.00 (BIO-PSA X7-4301) Styrene-isoprene-styrene 15.00 Polymer (Kraton D1107) Propylene Gylcol 5.00 Linoleic Acid 8.00 Lecithin 6.00 (Vitamin E Acetate) Haloperidol 10.00 100.00 DETD . . . Polysiloxane Adhesive 61.00 (BIO-PSA X7-4301) Ethylene/Vinyl Acetate 10.00 Polymer

(Elvax 40W)

```
Oleic Acid
                           6.00
      Tocopherol Acetate
                           3.00
       (Vitamin E Acetate)
      Haloperidol
                          20.00
                          100.00
DETD
               . . . Polysiloxane Adhesive 44.00
        (BIO-PSA X7-4301)
       Butyl Rubber
                         25.00
       Butylene Glycol
                         5.00
       Linoleic Acid
                         8.00
       Tocopherol Acetate 3.00
        (Vitamin E Acetate)
       Haloperidol
                         15.00
                         100.00
DETD
              . . PERCENT BY WEIGHT
      Polyacrylate Adhesive 55.00
      (GMS 737)
      Polyisobutylene
                        20.00
      Dipropylene Glycol 5.00
      Oleic Acid
      Polyvinylpyrrolidone 10.00
      (Kollidon 30)
      Haloperidol
                        100.00
ΙT
     50-27-1, Estriol 50-36-2, Cocaine 50-52-2, Thioridazine
     Chlorpromazine, biological studies 50-54-4, Quinidine sulfate
     51-06-9, Procainamide 51-83-2, Carbachol 51-84-3, Acetylcholine,
     biological studies 51-98-9, Norethindrone acetate 52-53-9, Verapamil
     52-76-6 52-86-8, Haloperidol 54-11-5, Nicotine 55-63-0,
     Nitroglycerin 55-92-5, Methacholine 56-53-1, Diethylstilbestrol
     57-63-6, Ethinyl estradiol 57-83-0, Progesterone, biological studies
     58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-74-2, Papaverine
     58-94-6, Chlorothiazide 58-95-7, Vitamin e acetate 59-46-1, Procaine
     62-49-7, Choline 68-22-4, Norethindrone 68-23-5, Norethynodrel
     68-96-2, 17\alpha-Hydroxyprogesterone 69-23-8, Fluphenazine
     71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol
     Benzhydroflumethiazide 76-57-3, Codeine 79-64-1, Dimethisterone
     84-06-0, Thiopropazate 85-79-0, Dibucaine 87-33-2, Isosorbide
     dinitrate 92c13-7, Pilocarpine 94-09-7, Benzocaine 94-24-6,
     Tetracaine 96-88-8, Mepivacaine 106-60-5, \delta-Aminolevulinic acid
     113-59-7, Chlorprothixene 117-89-5, Trifluoperazine 137-58-6,
     Lidocaine 146-54-3, Triflupromazine 152-62-5, Dydrogesterone
     297-76-7, Ethynodiol diacetate 300-54-9, Muscarine 434-03-7,
     Ethisterone 437-38-7, Fentanyl 439-14-5, Diazepam 472-54-8,
     19-Norprogesterone 474-86-2, Equilin 525-66-6, Propranolol
     586-06-1, MetaProterenol 586-60-7, Dyclonine 595-33-5, Megestrol
     acetate 604-75-1, Oxazepam 630-56-8, Hydroxypro-gesterone caproate
     674-38-4, Bethanechol 721-50-6, Prilocaine 846-49-1, Lorazepam
     1622-61-3, Clonazepam 1961-77-9, Chlormadinone 1977-10-2, Loxapine
     2180-92-9, Bupivacaine 2751-68-0, Acetophenazine 2955-38-6, Prazepam
     3313-26-6, Thiothixene 3819-00-9, Piperacetazine 4205-90-7, Clonidine
     5588-33-0, Mesoridazine 5633-18-1, Melengestrol 6533-00-2, Norgestrel
     7280-37-7, Estropipate 7416-34-4, Molindone 9003-39-8,
     Polyvinylpyrrolidone 10116-22-0, Demegestone 10457-90-6, Bromperidol
     13392-18-2, Fenoterol 13642-52-9, Soterenol 13757-97-6, Quinterenol
     14611-51-9, Selegiline 16051-77-7, Isosorbide mononitrate 17617-23-1,
     Flurazepam 18559-94-9, Albuterol 18910-65-1, Salmefamol 19216-56-9,
     Prazosin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 23031-25-6,
     Terbutaline 23092-17-3, Halazepam 23887-31-2, Clorazepate
     26839-75-8, Timolol 28911-01-5, Triazolam 28981-97-7, Alprazolam
     32953-89-2, Rimiterol 34184-77-5, Promegestone 34866-47-2, Carbuterol
     36637-18-0, Etidocaine 42399-41-7, Diltiazem 52485-79-7,
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55985-32-5, Nicardipine 62571-86-2, Captopril Buprenorphine (transdermal drug delivery system contg. polyvinylpyrrolidone as soly.

L13 ANSWER 13 OF 16 USPATFULL

Full-text

ACCESSION NUMBER:

1998:17360 USPATFULL

TITLE:

Compositions and methods for topical administration of

pharmaceutically active agents

INVENTOR(S):

Kanios, David P., Miami, FL, United States

Gentile, Joseph A., Plantation, FL, United States

Mantelle, Juan A., Miami, FL, United States Sablotsky, Steven, Miami, FL, United States

PATENT ASSIGNEE(S):

Noven Pharmaceuticals, Inc., Miami, FL, United States

(U.S. corporation)

NUMBER DATE

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.: US 5719197 19980217 US 1995-477361 19950607 (8)

Continuation-in-part of Ser. No. US 1993-112330, filed on 27 Aug 1993, now patented, Pat. No. US 5446070 which is a continuation-in-part of Ser. No. US 1991-813196,

filed on 23 Dec 1991, now patented, Pat. No. US 5234957

which is a continuation-in-part of Ser. No. US 1991-661827, filed on 27 Feb 1991, now abandoned , said Ser. No. US 1995-477361, filed on 7 Jun 1995 which is a continuation-in-part of Ser. No. US 1993-67001, filed on 26 May 1993 which is a continuation of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which is a continuation-in-part of Ser. No. US 1989-295847, filed on 11 Jan 1989, now patented, Pat. No. US 4994267 which is a continuation-in-part of

Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Azpuru, Carlos A.

Foley Lardner

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

27

1

LINE COUNT:

1799

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Compositions for topical application comprising a therapeutically effective amount of a pharmaceutical agent(s), a pharmaceutically acceptable bioadhesive carrier, a solvent for the pharmaceutical agent(s) in the carrier and a clay, and methods of administering the pharmaceutical agents to a mammal are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Butyrophenones such as Benperidol, Bromperidol, Droperidol, Fluanisone, DETD Haloperidol, Melperone, Moperone, Pipamperone, Sniperone, Timiperone, Trifluperidol

IT 50-27-1, Estriol 50-28-2, Estradiol, biological studies Estradiol, esters 50-70-4, Sorbitol., biological studies 51-98-9, Norethindrone acetate 52-76-6 53-16-7, Estrone, biological studies 56-53-1, Diethylstilbestrol 56-81-5, 1,2,3-Propanetriol, biological studies 57-55-6, 1,2-Propanediol, biological studies 57-63-6, Ethinyl estradiol; 57-83-0, Progesterone, biological studies 58-18-4, Methyltestosterone 58-22-0, Testosterone; 59-46-1, Procaine 68-22-4, Norethindrone 68-23-5, Norethynodrel 68-96-2, Hydroxyprogesterone 71-58-9, Medroxyprogesterone acetate; Mestranol 76-43-7, Fluoxymesterone; 79-64-1, Dimethisterone

85-79-0, Dibucaine 94-09-7, Benzocaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 107-21-1, 1,2-Ethanediol, biological studies 107-41-5, Hexylene glycol, 133-16-4, Chloroprocaine 137-58-6, Lidocaine 152-62-5, Dydrogesterone 297-76-7, Ethynodiol diacetate 472-54-8, 19-Norprogesterone 474-86-2, Equilin 586-60-7, Dyclonine 595-33-5, Megestrol acetate 630-56-8, Hydroxyprogesterone caproate 721-50-6, Prilocaine 979-32-8, Estradiol valerate 1961-77-9, Chlormadinone; 5633-18-1, Melengestrol 6533-00-2 7280-37-7, Estropipate 9000-30-0. Guar gum 9000-36-6, Karaya gum 9000-65-1, Tragacanth gum 9000-69-5, Pectin 9004-34-6, Cellulose, biological studies 10116-22-0, Demegestone 11138-66-2, Xanthan gum 22916-47-8, Miconazole. 23593-75-1, Clotrimazole. 25265-71-8, Dipropylene glycol 25265-75-2, Butylene glycol 25322-68-3 25322-69-4, Polypropylene glycol 34184-77-5, Promegestone 36637-18-0, Etidocaine 38396-39-3, Bupivacaine (topical pharmaceutical compns. comprising bioadhesive carrier, solvent

and clay)

## L13 ANSWER 14 OF 16. USPATFULL

Full-text

ACCESSION NUMBER: 97:70731 USPATFULL

TITLE:

Solubility parameter based drug delivery system and

method for altering drug saturation concentration

INVENTOR(S):

Miranda, Jesus, Miami, FL, United States Sablotsky, Steven, Miami, FL, United States

PATENT ASSIGNEE(S):

Noven Pharmaceuticals, Inc., Miami, FL, United States

(U.S. corporation)

US 5656286

NUMBER DATE -----

PATENT INFORMATION:

19970812

APPLICATION INFO.:

US 1994-178558 19940107 (8)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1991-722342, filed on 27 Jun 1991, now patented, Pat. No. US 5474783 which is a continuation-in-part of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which is a continuation-in-part of Ser. No. US

1989-295847, filed on 11 Jan 1989, now patented, Pat. No. US 4994267, issued on 19 Feb 1991 which is a

continuation-in-part of Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168,

issued on 21 Mar 1989

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Venkat, Jyothsna Foley Lardner

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

73

NUMBER OF DRAWINGS:

1,4 20 Drawing Figure(s); 19 Drawing Page(s)

LINE COUNT: 3344

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug provides a pressure-sensitive adhesive composition for a transdermal drug delivery system in which the drug is delivered from the pressure-sensitive adhesive composition and through dermis when the pressure-sensitive adhesive composition is in contact with human skin. According to the invention, soluble polyvinylpyrrolidone can be used to prevent crystallization of the drug, without affecting the rate of drug delivery from the pressure-sensitive adhesive composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

. . . as nitroglycerin. In still other embodiments, the drug is a

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cholinergic agent, such as pilocarpine, or an antipsychotic such as
       haloperidol or a tranquilizer/sedative such as alprazolam.
DETD
       Butyrophenones such as Benperidol, Bromperidol, Droperidol, Fluanisone,
       Haloperidol, Melperone, Moperone, Pipamperone, Sniperone, Timiperone
       and Trifluperidol;
        . . . substantially crystal-free. Other specific drugs for which
DETD
       soluble PVP is particularly usefully employed according to the invention
       include albuterol, estradiol, haloperidol and alprazolam.
DETD
EXAMPLE 72
COMPONENT
                 PERCENT BY WEIGHT
Polysiloxane Adhesive
                 56.00
(BIO-PSA X7-4301)
Styrene-isoprene-styrene
Polymer
(Kraton D1107)
Propylene Gylcol
                5.00
Linoleic Acid
                8.00
Lecithin
                6.00
(Vitamin E Acetate)
Haloperidol
                10.00
                100.00
DETD
EXAMPLE 73
COMPONENT
                PERCENT BY WEIGHT
Polysiloxane Adhesive
                61.00
(BIO-PSA X7-4301)
Ethylene/Vinyl Acetate
                10.00
Polymer
(Elvax 40W)
Oleic Acid
                6.00
Tocopherol Acetate
                3.00
(Vitamin E Acetate)
Haloperidol
                20.00
                100.00
DETD
EXAMPLE 74
COMPONENT
               PERCENT BY WEIGHT
Polysiloxane Adhesive
               44.00
(BIO-PSA X7-4301)
Butyl Rubber
               25.00
Butylene Glycol
Linoleic Acid 8.00
Tocopherol Acetate
               3.00
(Vitamin E Acetate)
Haloperidol
               15.00
               100.00
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DETD EXAMPLE 77 COMPONENT PERCENT BY WEIGHT Polyacrylate Adhesive 55.00 (GMS 737) Polyisobutylene 20.00 Dipropylene Glycol 5.00 Oleic Acid 8.00 Polyvinylpyrrolidone 10.00 (Kollidon 30) Haloperidol 2.00 100.00

- . antipsychotic is selected from the group consisting of thiopropazate, chlorpromazine, triflupromazine, mesoridazine, piperacetazine, thioridazine, acetophenazine, fluphenazine, perphenazine, trifluoperazine, chlorprathixene, thiothixene, haloperidol, bromperidol, loxapine and molindone.
- 43. The transdermal drug delivery system of claim 42, wherein said antipsychotic is haloperidol.
- IT 50-27-1, Estriol 50-36-2, Cocaine 50-52-2, Thioridazine Chlorpromazine, biological studies 50-54-4, Quinidine sulfate 51-06-9, Procainamide 51-83-2, Carbachol 51-84-3, Acetylcholine, biological studies 51-98-9, Norethindrone acetate 52-53-9, Verapamil 52-76-6 **52-86-8**, Haloperidol **54-11-5**, Nicotine **55-63-0**, Nitroglycerin 55-92-5, Methacholine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol 57-83-0, Progesterone, biological studies 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-74-2, Papaverine 58-94-6, Chlorothiazide 58-95-7, Vitamin e acetate 59-46-1, Procaine 62-49-7, Choline 68-22-4, Norethindrone 68-23-5, Norethynodrel **68-96-2**,  $17\alpha$ -Hydroxyprogesterone 69-23-8, Fluphenazine 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol Benzhydroflumethiazide 76-57-3, Codeine 79-64-1, Dimethisterone 84-06-0, Thiopropazate 85-79-0, Dibucaine 87-33-2, Isosorbide dinitrate 92-13-7, Pilocarpine 94-09-7, Benzocaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 106-60-5,  $\delta$ -Aminolevulinic acid 113-59-7, Chlorprothixene 117-89-5, Trifluoperazine 137-58-6, Lidocaine 146-54-3, Triflupromazine 152-62-5, Dydrogesterone 297-76-7, Ethynodiol diacetate 300-54-9, Muscarine 434-03-7, Ethisterone 437-38-7, Fentanyl 439-14-5, Diazepam 472-54-8, 19-Norprogesterone 474-86-2, Equilin 525-66-6, Propranolol 586-06-1, MetaProterenol 586-60-7, Dyclonine 595-33-5, Megestrol acetate 604-75-1, Oxazepam 630-56-8, Hydroxypro-gesterone caproate 674-38-4, Bethanechol 721-50-6, Prilocaine 846-49-1, Lorazepam 1622-61-3, Clonazepam 1961-77-9, Chlormadinone 1977-10-2, Loxapine 2180-92-9, Bupivacaine 2751-68-0, Acetophenazine 2955-38-6, Prazepam 3313-26-6, Thiothixene 3819-00-9, Piperacetazine 4205-90-7, Clonidine 5588-33-0, Mesoridazine 5633-18-1, Melengestrol 6533-00-2, Norgestrel 7280-37-7, Estropipate 7416-34-4, Molindone 9003-39-8, Polyvinylpyrrolidone 10116-22-0, Demegestone 10457-90-6, Bromperidol 13392-18-2, Fenoterol 13642-52-9, Soterenol 13757-97-6, Quinterenol 14611-51-9, Selegiline 16051-77-7, Isosorbide mononitrate 17617-23-1, Flurazepam 18559-94-9, Albuterol 18910-65-1, Salmefamol 19216-56-9, Prazosin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 23031-25-6,

CLM What is claimed is:

Terbutaline 23092-17-3, Halazepam 23887-31-2, Clorazepate 26839-75-8, Timolol 28911-01-5, Triazolam 28981-97-7, Alprazolam 32953-89-2, Rimiterol 34184-77-5, Promegestone 34866-47-2, Carbuterol 36637-18-0, Etidocaine 42399-41-7, Diltiazem 52485-79-7, 55985-32-5, Nicardipine 62571-86-2, Captopril Buprenorphine (transdermal drug delivery system contg. polyvinylpyrrolidone as soly. enhancer)

L13 ANSWER 15 OF 16 USPATFULL

Full-text

ACCESSION NUMBER:

95:110233 USPATFULL

TITLE:

Solubility parameter based drug delivery system and method for altering drug saturation concentration

INVENTOR (S):

Miranda, Jesus, Miami, FL, United States Sablotsky, Steven, Miami, FL, United States

PATENT ASSIGNEE(S):

Noven Pharmaceuticals, Inc., Miami, FL, United States

(U.S. corporation)

NUMBER DATE

PATENT INFORMATION:

US 5474783 19951212

APPLICATION INFO.:

US 1991-722342 19910627 (7)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which

is a continuation-in-part of Ser. No. US 1989-295847. filed on 11 Jan 1989, now patented, Pat. No. US

4994267, issued on 19 Feb 1991 which is a

continuation-in-part of Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168,

issued on 21 Mar 1989

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Denkat, Jyothsna

LEGAL REPRESENTATIVE:

Foley Lardner

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

32 1

NUMBER OF DRAWINGS:

15 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 1471

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The method of adjusting the saturation concentration of a drug in a transdermal composition for application to the dermis, which comprises mixing polymers having differing solubility parameters, so as to modulate the delivery of the drug. This results in the ability to achieve a predetermined permeation rate of the drug into and through the dermis. In one embodiment, a dermal composition of the present invention comprises a drug, an acrylate polymer, and a polysiloxane. The dermal compositions can be produced by a variety of methods known in the preparation of drug-containing adhesive preparations, including the mixing of the polymers, drug, and additional ingredients in solution, followed by removal of the processing solvents. The method and composition of this invention permit selectable loading of the drug into the dermal formulation and adjustment of the delivery rate of the drug from the composition through the dermis, while maintaining acceptable shear, tack, and peel adhesive properties.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM

. . . nitroglycerin. In still other embodiments, the bioactive agent is a cholinergic agent, such as pilocarpine, or an antipsychotic such as haloperidol or a tranquilizer/sedative such as alprazolam.

DETD

. . . action on the central nervous system, for example sedatives, hyponotics, antianxiety agents, analgesics and anesthetics, such as chloral, buprenorphine, naloxone, haloperidol, fluphenazine, pentobarbital, phenobarbital, secobarbital, codeine, lidocaine,

tetracaine, dyclonine, dibucaine, cocaine, procaine, mepivacaine, bupivacaine, etidocaine, prilocaine, benzocaine, fentanyl, and nicotine.

25. Antipsychotics, such as thiopropazate, chlorpromazine, triflupromazine, mesoridazine, piperacetazine, thioridazine, acetophenazine, fluphenazine, perphenazine, trifluoperazine, chlorprothixene, thiothixene, haloperidol, bromperidol, loxapine, and molindone.

CLM What is claimed is:

. chloramdinone, ethisterone, medroxyprogesterone acetate, hydroxyprogesterone caproate, ethynodiol diacetate, norethynodrel, 17-alpha-hydroxyprogesterone, dydrogesterone, dimethisterone, ethinylestrenol, norgestrel, demegestone, promegestone, megestrol acetate, buprenorphine, naloxone, haloperidol, codeine, lidocaine, tetracaine, dyclonine, dibucaine, cocaine, procaine, mepivacaine, bupivacaine, etidocaine, prilocaine, benzocaine, fentanyl, hydrocortisone, cortisone, prednisolone, prednisone, halcinonide, betamethasone, ibuprophen, . . .

an antipsychotic selected from the group consisting of thiopropazate, chlorpromazine, triflupromazine, mesoridazine, piperacetazine, thioridazine, acetophenazine, fluphenazine, perphenazine, trifluoperazine, chlorprothixene, thiothixene, haloperidol, bromperidol, loxapine and molindone.

24. The transdermal drug delivery system of claim 23, wherein the antipsychotic is haloperidol.

ΙT 50-27-1, Estriol 50-28-2, 17β-Estradiol, biological studies 50-52-2, Thioridazine 50-53-3, Chlorpromazine, 50-36-2, Cocaine biological studies 50-54-4, Quinidine sulfate 51-06-9, Procainamide 51-83-2, Carbachol 51-84-3, Acetylcholine, biological studies 51-98-9, Norethindrone acetate 52-53-9, Verapamil 52-76-6 52-86-8, Haloperidol 53-16-7, Estrone, biological studies 54-11-5, Nicotine 55-63-0, Nitroglycerin 55-92-5, Methacholine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol Progesterone, biological studies 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-94-6, Chlorothiazide 59-46-1, Procaine 63-75-2, Arecoline 68-22-4, Norethindrone 68-23-5, Choline Norethynodrel 68-96-2, 17-Hydroxyprogesterone 69-23-8, Fluphenazine 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 73-48-3, Bendroflumethiazide 76-57-3, Codeine 79-64-1, Dimethisterone 84-06-0, Thiopropazate 85-79-0, Dibucaine 87-33-2, Isosorbide dinitrate 92-13-7, Pilocarpine 94-09-7, Benzocaine 94-24-6, Tetracaine 95-88-8, Mepivacaine 113-59-7 117-89-5, Trifluoperazine 137-58-6, Lidocaine 146-54-3, Triflupromazine 152-62-5, Dydrogesterone 297-76-7, Ethynodiol diacetate 300-54-9, Muscarine 434-03-7, Ethisterone 437-38-7, Fentanyl 439-14-5, Diazepam 472-54-8, 19-Norprogesterone 474-86-2, Equilin 525-66-6, Propranolol 586-60-7, Dyclonine 586-06-1, Metaproterenol 595-33-5, Megestrol acetate 604-75-1, Oxazepam 630-56-8 721-50-6, Prilocaine 846-49-1, Lorazepam 1622-61-3, Clonazepam 1961-77-9, Chlormadinone 1977-10-2, Loxapine 2180-92-9, Bupivacaine 2751-68-0, Acetophenazine 2955-38-6, Prazepam 3819-00-9, Piperacetazine 4205-90-7, Clonidine 5588-33-0, Mesoridazine 5591-45-7, Thiothixene 5633-18-1, Melengestrol 6533-00-2, Norgestrel 7280-37-7, Estropipate 7416-34-4, Molindone 10116-22-0, Demegestone 10457-90-6, Bromperidol 13392-18-2, Fenoterol 13642-52-9, Soterenol 13757-97-6, Quinterenol 16051-77-7, Isosorbide mononitrate 17617-23-1, Flurazepam 18559-94-9, Albuterol 18910-65-1, Salmefamol 19216-56-9, Prazosin 21829-25-4, Nifedipine 23031-25-6, Terbutaline 23092-17-3, Halazepam 23887-31-2 26839-75-8, Timolol 28911-01-5, Triazolam 28981-97-7, Alprazolam 30418-38-3, Tretoquinol 32953-89-2, Rimiterol 34184-77-5, 34866-47-2, Carbuterol 36637-18-0, Etidocaine Promegestone

42399-41-7, Diltiazem 52485-79-7, Buprenorphine 55985-32-5, 62571-86-2, Captopril 91609-06-2, Betanechol (transdermal pressure-sensitive adhesive delivery system for, controlled-release)

L13 ANSWER 16 OF 16 USPATFULL

Full-text

ACCESSION NUMBER:

93:65429 USPATFULL

TITLE:

Compositions and methods for topical administration of

pharmaceutically active agents

INVENTOR(S):

Mantelle, Juan A., Miami, FL, United States

PATENT ASSIGNEE(S): .

Noven Pharmaceuticals, Inc., Miami, FL, United States

(U.S. corporation)

NUMBER DATE \_\_\_\_\_\_

PATENT INFORMATION:

US 5234957 19930810

APPLICATION INFO.:

US 1991-813196 19911223 (7)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1991-661827, filed

on 27 Feb 1991, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER: ASSISTANT EXAMINER: Page, Thurman K. Azpuru, Carlos

LEGAL REPRESENTATIVE:

Foley Lardner

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

LINE COUNT: 1218

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A composition for topical application comprising a therapeutically effective amount of a pharmaceutical agent(s), a flexible, finite, pharmaceutically acceptable, bioadhesive carrier, and a solvent for the pharmaceutical agent(s) in the carrier and a method of administering the pharmaceutical agent to a mammal are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

. . . action on the central nervous system, for example sedatives, hypnotics, antianxiety agents, analgesics and anesthetics, such as, chloral, buprenorphine, naloxone, haloperidol, fluphenazine, pentobarbital, phenobarbital, secobarbital, amobarbital, cydobarbital, codeine, lidocaine, tetracaine, dyclonine, dibucaine, cocaine, procaine, mepivacaine, bupivacaine, etidocaine, prilocaine, benzocaine, fentanyl, nicotine,. .

DETD . . phenothiazines including thiopropazate, chlorpromazine, triflupromazine, mesoridazine, piperracetazine, thioridazine, acetophenazine, fluphenazine, perphenazine, trifluoperazine, and other major tranqulizers such as, chlorprathixene, thiothixene, haloperidol, bromperidol, loxapine, and molindone, as well as, those agents used at lower doses in the treatment of nausea, vomiting, and. .

IT 50-27-1, Estriol 50-28-2,  $17\beta$ -Estradiol, biological studies 51-98-9, Norethindrone acetate 52-76-6 53-16-7, Estrone, biological studies 56-53-1, Diethylstilbestrol 57-63-6 57-83-0, Progesterone, biological studies 58-18-4, Methyltestosterone 58-22-0, Testosterone 59-46-1, Procaine 68-22-4, Norethindrone 68-23-5, Norethynodrel 68-96-2,  $17\alpha$ -Hydroxyprogesterone 71-58-9,

Medroxyprogesterone acetate 72-33-3, Mestranol 76-43-7, Fluoxymesterone 79-64-1, Dimethisterone 85-79-0, Dibucaine Benzocaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 133-16-4, Chloroprocaine 136-47-0, Tetracaine hydrochloride 137-58-6, Lidocaine 152-62-5, Dydrogesterone 297-76-7, Ethynodiol diacetate 472-54-8, 19-Norpregn-4-ene-3,20-dione 474-86-2, Equilin 536-43-6, Dyclonine hydrochloride 586-60-7, Dyclonine 595-33-5, Megestrol acetate 630-56-8 721-50-6, Prilocaine 979-32-8, 17β-Estradiol valerate

1722-62-9, Mepivacaine hydrochloride 1786-81-8, Prilocaine hydrochloride 1961-77-9, Chlormadinone 2180-92-9, Bupivacaine 5633-18-1, Melengestrol 6533-00-2, Norgestrel 7280-37-7, Estropipate 10116-22-0, Demegestone 18010-40-7, Bupivacaine hydrochloride 34184-77-5, Promegestone 36637-18-0, Etidocaine (topical formulation of)

=> index bioscience FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED COST IN U.S. DOLLARS

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
102.19
118.98

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION
CA SUBSCRIBER PRICE

-5.29
-5.29

INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, ...' ENTERED AT 00:36:21 ON 11 JUN 2001

59 FILES IN THE FILE LIST IN STNINDEX

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- => s 16 and (14 or 15)
  - 0\* FILE ADISALERTS
  - 0 \* FILE ADISINSIGHT
  - 0\* FILE AGRICOLA
  - 0\* FILE ANABSTR
  - 0\* FILE AQUASCI
- => s 16 and (14 or 15)
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  - 0 \* FILE ADISINSIGHT
  - 0 \* FILE AGRICOLA
  - 0 \* FILE ANABSTR
  - 0 \* FILE AQUASCI
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  - 0\* FILE ADISINSIGHT
  - 0 \* FILE AGRICOLA
  - 0 \* FILE ANABSTR